

From THE INSTITUTE OF ENVIRONMENTAL MEDICINE
Karolinska Institutet, Stockholm, Sweden

**DEEP TISSUE MASSAGE THERAPY AND/OR STRENGTHENING AND STRETCHING
EXERCISES FOR DISABLING SUBACUTE OR CHRONIC NECK PAIN.
A RANDOMIZED CONTROLLED TRIAL**

Oscar Javier Pico Espinosa



**Karolinska
Institutet**

Stockholm 2020

All previously published papers were reproduced with permission from the publisher.

Published by Karolinska Institutet.

Printed by Eprint AB 2020

© Oscar Javier Pico Espinosa, 2020

ISBN 978-91-7831-661-8

DEEP TISSUE MASSAGE THERAPY AND/OR STRENGTHENING AND STRETCHING
EXERCISES FOR DISABLING SUBACUTE OR CHRONIC NECK PAIN. A RANDOMIZED
CONTROLLED TRIAL

THESIS FOR DOCTORAL DEGREE (Ph.D.)

By

Oscar Javier Pico Espinosa

Principal Supervisor:

Professor Eva Skillgate
Karolinska Institutet
Institute of Environmental Medicine
Unit of Intervention and Implementation

Co-supervisor(s):

Associate Professor Lena W. Holm
Karolinska Institutet
Institute of Environmental Medicine
Unit of Intervention and Implementation

Professor Irene Jensen
Karolinska Institutet
Institute of Environmental Medicine
Unit of Intervention and Implementation

Opponent:

Professor Jan Hartvigsen
University of Southern Denmark
Department of Sports Science and Clinical
Biomechanics
Division of Clinical Biomechanics

Examination Board:

Associate Professor Monika Löfgren
Karolinska Institutet
Department of Clinical Sciences, Danderyd
Hospital
Division of Rehabilitation Medicine

Professor Peter Lindgren
Karolinska Institutet
Department of Learning, Informatics, Management
and Ethics
Division of Medical Management

Professor Andreas Holtermann
University of Southern Denmark and National
Centre for the Working Environment
Copenhagen, Denmark

Preface

Health is freedom of action; is having a positive and enriching life; and is having a good enough physical and psychological functioning.¹ However... “If you are to define it as the society, then you have to be seriously ill to be seen as sick. You must have cancer or some very serious disease. To be considered as sick, anyway, you can’t have back pain, pain in your shoulders or something like that. Then you will be considered as being well and able to manage things”¹

¹ Wiitavaara B, Bengs C, Brulin C. Well, I’m healthy, but... - lay perspectives on health among people with musculoskeletal disorders. *Disabil Rehabil.* 2016;38(1): 71-80. doi:10.3109/09638288.2015.1024338.

ABSTRACT

Background

Neck pain is a common condition responsible for a significant amount of disability worldwide. Various treatment modalities are used to manage neck pain, but evidence supporting their use is scarce, conflicting or of low quality.

Objectives

The aim of this thesis is to present the results of the Stockholm Neck (STONE) trial, a four-arm randomized controlled trial of 619 participants with disabling subacute or chronic neck pain who were followed up to one year. The objectives of the STONE trial were to determine the effectiveness, safety profile and cost-effectiveness of deep tissue massage, strengthening and stretching exercises and a combined therapy including both components, in comparison to advice to stay active. Moreover, additional information was collected with the objective of describing the course of the condition over time.

Methods

In **Study I**, different trajectories of the course of neck pain as well as baseline variables associated with unfavorable trajectories were identified. **Study II** was an analysis aiming to determine the effect of deep tissue massage, strengthening and stretching exercises and a combined therapy including both components, using advice to stay active as a reference group. Two primary outcomes: pain intensity and pain-related disability, and two secondary outcomes: self-perceived recovery and sickness absence, were measured at 7, 12, 26 and 52 weeks. In **Study III**, participants were asked to report and describe adverse events debuting after the sessions of therapy. That information was contrasted against the proportion of participants in each group achieving perceived recovery at seven weeks, in order to calculate measures of harm in relation to benefits. In **Study IV**, costs resulting from neck pain were estimated, including those directly and indirectly related to the interventions given in the STONE trial. The costs associated with gains in health-related quality of life due to the given interventions were calculated.

Results

In **Study I**, six different trajectories were identified, and a quarter of participants had unfavorable courses of neck pain characterized by high pain intensity, either constant or fluctuating. High pain intensity at baseline, being a woman and having depressive symptoms at baseline were among the factors associated with such unfavorable courses. In **Study II**, compared to advice, massage alone or in combination with exercise resulted in less minimal clinically important improvement (MCII) in pain intensity in the short term, and exercise alone resulted in less MCII in pain intensity in the mid-term. Massage and/or exercise resulted in similar MCII in pain intensity compared to advice in the long term. Moreover, no differences were observed between treatment arms for MCII in pain-related disability or sickness absence after one year. On the other hand, compared to advice, all the other

therapies resulted in better self-perceived recovery. In **Study III**, it was found that around a third of participants reported adverse events that were classified as highly bothersome. The most common adverse events were tiredness, muscle soreness, increased pain and stiffness. None of the adverse events were serious. No clear differences between treatment arms were observed in terms of harms in relation to benefits. In **Study IV**, massage alone or combined with exercise were found to be more costly and resulting in less gains of quality of life than advice. Exercise, on the other hand, was found to be cost-effective compared to advice to stay active.

Discussion and conclusions

Non-specific neck pain is a subjective, individual and complex experience. Therefore, evaluations of interventions should consider the interplay of various biological and psychosocial factors. Compared to advice, massage and exercise therapy are associated with modest effects in terms of minimal clinically important improvement in pain intensity and no effects in minimal clinically important improvement in pain-related disability. However, improvements in other dimensions of pain – that were probably captured by the outcome “perceived recovery” – result from the mentioned interventions. Furthermore, the therapies are safe, and exercise seems to be cost-effective compared to advice.

The STONE trial used a rigorous procedure to ensure a proper randomization and allocation concealment. Despite blinding participants not being possible, well-defined criteria to assess the outcomes were followed. In addition, significant efforts were made to provide the therapies according to pre-established protocols and to achieve high response rates. Appropriate methods for the analysis of the data were followed. All these elements combined ensure the internal validity of the trial.

The STONE trial is a predominantly pragmatic trial, while aspects such as intensive measurement and the use of a single center for the provision of the therapies correspond more to an explanatory trial, a good balance between rigorousness and pragmatism was achieved. This balance allows the results from this trial to be generalized to populations with subacute and persistent non-specific neck pain.

LIST OF SCIENTIFIC PAPERS

- I. Pico-Espinosa OJ, Côté P, Hogg-Johnson S, Jensen I, Axén I, Holm LW, Skillgate E. Trajectories of pain intensity over 1 year in adults with disabling subacute or chronic neck pain. Clin J Pain. 2019 Aug;35(8):678-685. doi: 10.1097/AJP.0000000000000727.
- II. Skillgate E & Pico-Espinosa OJ, Côté P, Jensen I, Viklund P, Bottai M, Holm LW. Effectiveness of deep tissue massage therapy, and supervised strengthening and stretching exercises for subacute or persistent disabling neck pain. The Stockholm Neck (STONE) randomized controlled trial. Musculoskelet Sci Pract. 2019 Oct 14;45:102070. doi: 10.1016/j.msksp.2019.102070.
- III. Pico-Espinosa OJ, Côté P, Jensen I, Holm LW, Skillgate E. Adverse events associated with deep tissue massage and supervised strengthening and stretching exercise in the treatment of subacute or persistent disabling neck pain. [Manuscript]
- IV. Pico-Espinosa OJ, Aboagye E, Côté P, Peterson A, Holm LW, Jensen I, Skillgate E. Deep tissue massage, strengthening and stretching exercises, and a combination of both compared with advice to stay active for subacute or persistent non-specific neck pain: a cost-effectiveness analysis of the Stockholm Neck trial (STONE). [Manuscript]

CONTENTS

1	Introduction	7
2	Background.....	9
	2.1. Current scientific evidence on the interventions in STONE.....	9
	2.2. Massage technique	11
	2.3. Exercises.....	12
	2.4. Advice to stay active	13
3	Aims.....	15
4	Subjects and methods.....	16
	4.1. Study design, setting and participants	16
	4.2. Sequence generation, randomization and allocation concealment	17
	4.3. Interventions	18
	4.3.1. Massage	18
	4.3.2. Exercise	18
	4.3.3. Massage and exercise.....	25
	4.3.4. Advice.....	25
	4.4. Follow-up and measurements	26
	4.5. Analyses	30
	4.5.1. Study I.....	30
	4.5.2. Study II	31
	4.5.3. Study III.....	32
	4.5.4. Study IV.....	33
5	Results	35
	5.1. Inclusion of participants.....	35
	5.2. Population characteristics	36
	5.3. Study I	36
	5.4. Study II	38
	5.4.1. Primary outcomes.....	38
	5.4.2. Secondary outcomes.....	39
	5.5. Study III.....	42
	5.6. Study IV.....	45
6	Discussion.....	47
	6.1 Main findings.....	47
	6.2 Methodological considerations	48
	6.2.1. Describing the disease: trajectories of neck pain	48
	6.2.2. Post-randomization factors. Should they be considered?	48
	6.2.3. Potential sources of bias in randomized controlled trials.....	53
	6.2.4. Generalizability of the findings from the STONE trial.....	58
	6.2.5. Additional considerations	62
	6.3. Summary of findings.....	63

	6.3.1. Messages for persons with non-specific neck pain	64
	6.3.2. Messages for health professionals and decision-makers.....	65
7	Ethical considerations	67
8	Conclusions	69
9	Future perspectives.....	70
10	Acknowledgements	71
11	References	73
12	Appendices	83

LIST OF ABBREVIATIONS

AE	Adverse event
AT	Advice therapy
CT	Combined therapy
EMS	Electrical muscle stimulation
ET	Exercise therapy
HADS	Hospital anxiety and depression scale
LCMM	Latent class mixed model
LHH	Likelihood of being helped versus harmed
M	Muscle
MT	Massage therapy
NNH	Number needed to harm
NNT	Number needed to treat
NP	Neck pain
NSAID	Non-steroid anti-inflammatory drug
RD	Risk difference
RR	Risk ratio
SD	Standard deviation
STONE	Stockholm Neck (trial)
TENS	Transcutaneous electrical nerve stimulation
TLV	The Swedish Dental and Pharmaceutical Benefits Agency

1 INTRODUCTION

Pain is an unpleasant and emotional experience associated with actual or potential tissue damage, or described in terms of such damage, and it is always subjective.² Pain might progress from being a symptom to being a disease. Classically described mechanisms behind such transition include lowering of the threshold for the activation of neural pathways responsible for pain, central sensitization derived from sustained periods of stimulation by noxious stimuli, and structural and functional neuronal changes.³

Neck pain refers to a condition in which a person perceives pain substantially in the neck area, without necessarily implying that the origin of pain is in the structures localized in the neck. Pain in the shoulders or a portion of the upper arm(s) may accompany the condition.⁴ Neck pain may result from fractures, infections, tumors, bone disease, arthritis, anatomic abnormalities, dysfunction or injury of specific structures of the neck or be of uncertain origin.⁴ In this thesis, I have focused on the latter, here referred as nonspecific neck pain.

Neck pain is a very common condition in Sweden and worldwide.⁵ The estimated point prevalence of neck pain is 4.9%⁶ and the annual prevalence lies between 15% and 50%.⁷ Its annual incidence is from 4% to 7%.⁸ It is among the leading causes of disability worldwide and its impact is, in particular, higher among the working population⁹ which translates into high costs for the society given the loss in productivity.^{8,10} Risk factors for nonspecific neck pain are older age, female sex, smoking, depressed mood, poor endurance of cervical extensor muscles and inefficiency in endogenous pain modulatory pathways.^{11–13} Biological or clinical prognostic factors for neck pain include female sex, older age, neck pain intensity at baseline, long duration of neck pain, pain in other areas of the body and lifestyle behaviors. Psychosocial characteristics such as recovery expectations, somatization, catastrophizing, sleep disturbances, social support and job strain are also important prognostic factors.^{8,14–18}

Neck pain is classified according to the duration of the symptoms as acute (less than 30 days), subacute (from 30 to less than three months) and chronic (three months or longer)¹⁹. This thesis focuses on subacute and chronic neck pain, also referred to as persistent neck pain.

Approximately a quarter of individuals experiencing persistent neck pain do not seek care and among those who do, the first provider they visit is often a primary care doctor.²⁰ As a consequence of this, there is an increased risk of relying on pharmacological strategies such

as opioids.²¹ In addition, a range of alternative or complementary therapeutic options with the potential of positive effects might not be offered to the patient, decreasing the opportunity to treat different components of the pain symptomatology. Although efforts are being made to fill knowledge gaps and change these practices²², more understanding is needed regarding the effect of certain interventions and the guidelines for treatment.

2 BACKGROUND

In the past few decades, there has been a shift from clinical practice based on unsystematic clinical experience and intuition and limited to reasoning from basic science, towards evidence-based practice. Although the ‘new’ paradigm recognizes the value of clinical experience, intuition and reasoning, it goes a step further by recognizing the fundamental need for high-quality clinical trials and observational studies.²³ Despite some challenges, there is agreement regarding the high value of evidence-based practice.²⁴ Unfortunately, given the lack of high-quality evidence, evidence-based practice has yet to further develop in some areas of healthcare, particularly for alternative or complementary non-pharmacological interventions.

Previous reports often claim a lack of high-quality evidence on interventions for chronic neck pain,¹⁰ including information on effectiveness and harms. Furthermore, evaluation of interventions from an economic perspective is fundamental for informing decision makers and the wider society. To achieve the aim of filling the gap in knowledge, high-quality studies should be designed, and the findings should be interpreted using methodological considerations.

The interventions compared in the STONE trial can be considered, to some extent, complex.²⁵ This means that an evaluation should take into consideration such complexity. Nonetheless, despite possible methodological particularities, the standards for such evaluation should be as high as for simpler interventions.²⁶

2.1. Current scientific evidence on the interventions in STONE

Literature on neck pain has evolved from a classical medical approach in which the aim was to find the anatomical cause of neck pain by imaging or clinical testing as well as limited therapeutic options,^{27,28} to a growing body of evidence on the effectiveness of non-pharmacological and complementary treatments.^{29,30}

The Swedish clinical guidelines for the management of nonspecific neck pain, updated in 2015³¹, recommend the following actions: return to normal activities from the debut of the condition, advice and analgesics. The first line of treatment is paracetamol, followed by a Non-steroid anti-inflammatory drug (NSAID) alone or in combination with paracetamol, and the third line is paracetamol plus codeine or tramadol. Benzodiazepines can be added to the

treatment regime during the acute phase, but they can also be useful later on during non-acute stages. When it comes to “other interventions”, the guidelines highlight the large variety of interventions and the conflicting evidence. Namely, the recommendations are: I) for general neck pain; home exercises are superior to analgesics only; exercise combined with manual therapy is equal to manipulation and mobilization; manipulation is superior to mobilization; advice combined with exercise is equal to the combination of advice, exercise and manual therapy, and to the combination of advice, exercise and short-wave therapy. II) Specifically for patients with long-lasting neck pain, in addition to the previous recommendations: education, mobilization or exercise are superior to usual care for whiplash-associated disorders; and supervised manual therapies, laser therapy or acupuncture are superior to no treatment or sham.³¹

International teams of reviewers established algorithms of more specific recommendations, listing therapies to be considered, always in combination with advice to stay active and reassurance.^{30,32,33} Such recommendations include: supervised range of motion combined with strengthening exercises, supervised qigong exercises, Iyengar yoga, a combination of a range of motion exercises with manipulation or mobilization, clinical massage, low-level laser therapy or NSAIDs. On the other hand, the following strategies are not recommended: high dose strengthening exercises only, strain-counterstrain, relaxation massage, transcutaneous electrical nerve stimulation (TENS), electrical muscle stimulation (EMS), pulsed shortwave diathermy, heat, electroacupuncture needles, botulinum toxin injections or acetaminophen only.

The commonly used deep tissue massage technique is often referred to in Sweden as Swedish massage. In some cases, Swedish massage is placed in the category of relaxation massage, rather than in the clinical massage category.³⁰ This interchangeability of terms results in a lack of clarity on its evidence, since, unlike the latter, relaxation massage is not recommended. In addition, the most recent Cochrane review on massage (in general) for neck pain concluded that such an intervention is safe but no effectiveness can be established based on the existing literature due to low quality and poor definitions.³⁴ On the other hand, there is evidence that supports the use of strengthening and endurance exercises.³⁵ Although there is evidence that supports the combination of exercise with some manual therapies (e.g. manipulation or mobilization techniques), there are no studies on the specific combination of deep tissue massage with strengthening and stretching exercises.³⁰

Evidence from 2012 suggested that education is ineffective for the treatment of neck pain.³⁶ In a review on persistent whiplash-associated disorders from 2016, advice alone was shown to have the same effect as advice together with physiotherapy or physiotherapy alone. For persistent neck pain, a mailed self-care book was shown to be less effective than massage therapy and, finally, e-mailed information on health behaviors was found to be less effective than exercises.³⁷

Evidence regarding the cost-effectiveness of certain interventions for chronic neck pain is also inconclusive.³⁸ One study evaluating light massage found that it might be cost-effective compared to a waiting list.³⁹ On the other hand, the literature suggests that classic massage is not cost-effective for back pain when provided alone compared to exercises.⁴⁰ However, this may not necessarily apply to neck pain. Evidence on the cost-effectiveness of supervised exercises for chronic neck pain is mixed. One study indicated that they might be cost-effective for neck pain if compared to usual care⁴⁰ and another found that they might be cost-effective when provided alone, but not when provided together with a behavioral intervention.⁴³ Another study found that it might be more expensive and less beneficial than home exercises or manual therapy.⁴¹ Finally, one session of education was shown to be cost-effective for whiplash-associated disorders.⁴⁴

There is a current scarcity of studies on adverse events of non-pharmacological interventions, which are limited to anecdotal information or a description of often unsystematically recorded adverse events. Described adverse events for therapies for neck pain include muscle soreness, tiredness, headache, migraine, stiffness, vertigo, dizziness, nausea, pain in other locations, hearing deteriorations or trauma.^{45–54}

2.2. Massage technique

Massage consists of a group of techniques involving myofascial stimulation, effleurage, deep stripping techniques and static compression. Techniques such as manipulation or mobilization are not part of this treatment modality.⁵⁵

There are upwards of 80 different forms of massage and, therefore, the field is characterized by lack of uniformity in the terminology used. This affects the reproducibility of techniques in practice and in research protocols aiming to generate evidence.⁵⁶ A specific type of massage may cover different techniques, which was the case in the present RCT. The STONE trial used “deep tissue massage” and combined elements from Swedish massage and clinical massage. The deep tissue massage used in the STONE trial consists of a combination

of the following techniques: effleurage, petrissage, friction, tapotement and management of trigger points. These techniques are often used in sports medicine during the preparation of or in-between or after competitions, and its use has traditionally been motivated more by beliefs rather than by existing evidence.⁵⁷

The proposed mechanisms of action of massage include; biomechanical, by decreasing adhesions between tissues leading to less stiffness in the muscle-tendon unit; and physiological, by increased muscle temperature and blood flow, or by reducing cortisol levels and increasing parasympathetic activity. The evidence on the latter is, however, somewhat weak.⁵⁷ Additional possible mechanisms include neurological mechanisms, by reducing neuromuscular excitability measured by H-reflex, and psychophysiological mechanisms, by enhancing the release of endorphins and decrease the level of arousal.⁵⁷ However, animal studies have been unable to show effects beyond short-term changes in the configuration of the muscle fibers or in levels of biological markers.⁵⁸

2.3. Exercises

Exercise, on the other hand, has been more widely studied and it is accepted that many mechanisms are responsible for achieving its beneficial effects. Such mechanisms include endogenous opioid and adrenergic mediated analgesia, the release of growth factors and the activation of supra-spinal nociceptive inhibitory pathways.⁵⁹ However, results from experimental studies on patients with widespread pain or whiplash-associated disorders may in fact report increased pain intensity or higher chance of flares after aerobic exercise sessions, probably as a characteristic of existing central sensitization, explained by excessive levels of nitric oxide and accounting for only certain musculoskeletal disorders.⁵⁹ On the other hand, patients with chronic low back pain do not appear to exhibit such negative effects. The latter does not suggest that exercise should not be a therapeutic option, but rather that attention should be paid to individual patients' responses and to give enough time to recover.^{59,60} Additionally, specific structural changes have been seen in the neck musculature of persons with chronic neck pain, leading to reduced activation or less defined activation patterns. Based on this, training of strength and endurance of specific muscle groups is recommended.⁶¹

Different types of exercises have been studied for the management of non-specific chronic neck pain, including craniocervical flexion exercises, cervical flexion exercises, strengthening exercises, isometric exercises, proprioception exercises, stretching exercises, range of motion

and flexibility exercises, yoga, qigong and general exercise.^{32,62} The STONE trial used a combination of craniocervical exercises, isometric exercises, strengthening exercises for the muscles of the neck, chest and scapula, and stretching exercises of the neck, chest, scapula and jaw. In addition to the supervised sessions, participants were told to repeat exercises at home.

2.4. Advice to stay active

Patient education aims for patients to acquire or maintain knowledge and skills to manage their condition in the best possible way through independence of care and self-management.³⁶ Advice refers to all information in any form that a patient receives and it is widely used within physiotherapy trials, and it can be given alone or in combination with another therapeutic program.⁶³ In general, evidence under the umbrella term ‘advice’ or ‘education’ often includes various techniques (for either acute or chronic neck pain) such as educational videos, pamphlets, generic information sessions in the emergency room, workplace ergonomics, and stress-coping skills and self-care strategies. However, these interventions often consist of one session only and are not based on learning theories but rather on mere information transfer. Common components of advice used in such trials include: advice to stay active and advice to exercise, education about pain and its mechanisms, information about prognosis and self-care strategies, stress-coping skills, general health information and ergonomic advice.³⁷

In the STONE trial, the control group consisted of oral and written information, mainly offering advice to stay active and advice to exercise, and was accompanied by information on stress-coping skills, the importance of engaging in social and leisure activities, self-care strategies and general health. The underlying assumption during the design of the study was that this was the best strategy to compare against.

3 AIMS

The overall aim of this thesis is to evaluate different aspects of three modalities of treatment for nonspecific chronic neck pain: deep tissue massage, strengthening and stretching exercises and a combination of deep tissue massage and strengthening and stretching exercises, and to describe the course of the condition. Specific aims are:

- To identify the one-year pain trajectories of individuals suffering from disabling subacute or persistent neck pain enrolled in a clinical trial; and to estimate the association between the observed one-year trajectory patterns and the following factors: age, sex, duration of neck pain, type of onset of neck pain, intensity of neck pain, depressive symptoms and treatment arm.
- To compare the effectiveness of deep tissue massage, supervised strengthening exercise and stretching, and a combined therapy (exercise followed by deep tissue massage) versus advice to stay active in persons with subacute or persistent neck pain.
- To describe the incidence of adverse events due to deep tissue massage, supervised strengthening and stretching exercises, and a combination of massage and exercise for subacute and chronic neck pain, and to compare the benefit-harm profile of these interventions.
- To examine the cost-effectiveness of deep tissue massage, strengthening and stretching exercises, or a combination of both in comparison to advice to stay active for subacute and chronic non-specific neck pain from a societal perspective.

4 SUBJECTS AND METHODS

4.1. Study design, setting and participants

The Stockholm neck (STONE) randomized controlled trial (RCT) was planned and designed between 2012 and 2014 and registered on the ISRCTN registry on July 3, 2014. The central hypothesis was that deep tissue massage and/or supervised strengthening exercise and stretching would lead to greater reduction in pain intensity, pain-related disability and improvement in perceived recovery and a lower risk of sickness absence. Participants were randomized to one of the following treatments: (1) deep tissue massage alone, (2) strengthening and stretching exercises alone, (3) deep tissue massage in combination with strengthening and stretching exercises, or (4) advice to stay active. The study was advertised on free circulation newspapers in Stockholm. Potential study participants contacted a study coordinator, who applied a questionnaire by telephone ('questionnaire A') in order to assess the following inclusion criteria, all based on self-reported information:

- Age equal or older than 18 years
- Pain lasting at least 30 days
- Pain intensity of at least 2/10 on a numeric rating scale
- Pain-related disability of at least 1/10 on a numeric rating scale
- Possession of a smartphone with access to the internet
- Able to communicate in Swedish
- No history of cancer in the past five years
- Not pregnant
- No severe skin disorders
- No treatment received by manual therapist in the past months
- No spinal fractures
- No spinal stenosis
- No arthritis in the spine area
- No osteoporosis
- No neck trauma in the past 48 hours
- No severe night pain
- No current use of corticosteroids
- No current drug abuse
- No signs of infection
- No neck pain debuting after 55 years old

4.2. Sequence generation, randomization and allocation concealment

A study coordinator prepared 800 sequentially numbered empty envelopes. Blocks of 160 pieces of paper (40 pieces for each of the four treatment arms) were prepared, folded and placed in a black bag. The pieces of paper were drawn, placed in the numbered envelopes one at a time, and sealed. This procedure was repeated five times until all the envelopes were filled. Folders were prepared with general information, a numbered blank questionnaire ('questionnaire B') and a numbered envelope. These folders were transported to the clinic of the Scandinavian College of Naprapathic Manual Medicine.

When a potential participant contacted the research team by e-mail, the study coordinator first confirmed that all the inclusion criteria were met ('questionnaire A') and when the participant had given their informed consent, they were then consecutively assigned a number from 1 to 800. The study coordinator booked an appointment with one of the 30 therapists of the study and registered the assigned number on the online booking system. When the study participants came to the study clinic, the therapist identified the number on the online system and assigned the corresponding numbered folder.

The therapists were licensed naprapaths² or 3rd or 4th year students at the Scandinavian College of Naprapathic Manual Medicine with previous experience with massage and physical exercises. All therapists received specific training on the procedures of the trial and the therapies during two three-hour sessions prior to the start of the study. Regular meetings with the therapists were held for repetition and questions raised by the therapists.

When the potential participants attended the clinic for the first time, they filled out 'questionnaire B'. The therapist conducted a clinical interview and a clinical examination to confirm the eligibility of the participants. If the participant was deemed eligible, the therapist opened the pre-assigned envelope, revealed the treatment arm to which the participant was randomly assigned and officially included the participant in the trial. The folder was archived if a potential participant did not attend the appointment with the therapist (even after sending reminders), was considered ineligible after the examination or they refused to be included in the trial (before the allocated treatment was revealed).

² Naprapaths are medical professionals who treat conditions of the musculoskeletal system.

4.3. Interventions

Participants were randomized to one of the following treatments: (1) deep tissue massage alone, (2) strengthening and stretching exercises alone, (3) deep tissue massage in combination with strengthening and stretching exercises, or (4) advice to stay active. The following description of the interventions can also be found in the appendix of Study I.⁶⁴

4.3.1. Massage

A maximum of six sessions of therapy during the course of six weeks were recommended: twice a week for the first week and less often thereafter. The visits lasted 45 minutes and at least 35 minutes were dedicated to active treatment at every session. Good rapport with the patient was encouraged.

Therapists started by applying an effleurage technique to the whole back and neck, followed by petrissage, kneading and edging/scissoring. Dynamic stretching as a component of myofascial release technique could be applied as part of the treatment. After general treatment of the neck and back, the therapist focused on the most affected/sore areas. The intensity of the pressure applied during the massage was adjusted according to the patient's status/willingness. The massage had to be experienced as appropriate and as beneficial without reaching more than 5/10 in a numeric rating scale of pain. The participants were told that they could request adjustments in the intensity of the massage at any given time. Thorax and/or jaw musculature was treated if indicated.

Pressure on tender points in the soft tissue was applied with a focus on the area that produced concordant signs (management of trigger points). Pressure on such areas was repeated with three increments of pressure applied at every decrease of the pain. If there was no decrease in pain, the pressure was sustained for 30 seconds. Myofascial techniques with and without active movement participation were combined with the techniques described above.

4.3.2. Exercise

A maximum of six sessions of therapies for six weeks were recommended: twice a week the first week and less often thereafter. The visits lasted 45 minutes and at least 35 minutes dedicated to active treatment at every session.

The program focused on activation of muscles of the neck area. The patient performed all exercises, but their intensity was adjusted to one of three levels (described below) depending on the patient's physical condition, tolerance and ability to perform. This assessment (points

1 and 2) was also the basis to decide whether the participant could progress to the next intensity level in the exercises.

1. Participant's performance:

The participant should perform the exercise correctly with minimal co-activation of other muscles/movements. The aim was that the participant performed the specified exercises in 3 x 10 repetitions if no other instruction was given.

2. Pain experienced by the participant:

The exercises should not produce pain over 5/10 in a visual analogue scale and the neck pain should not increase the day after training by more than two points on the same scale.

The participant was instructed to perform the exercises at home one to two times per week doing 3 x 10 with good technique. In order to achieve this, the participant was filmed with their smartphone during the first supervised session, and the therapist indicated with verbal instructions what was important to consider during the execution of the exercises.

Specific description of the exercises:

1-Activation of deep neck flexors ("The owl")

- Purpose: to activate and strengthen deep cervical flexors (M. longus colli and M. rectus capitis anterior) for increased cervical strength and/or neck function.
- Considerations: minimize pressure of extensors, avoid compensation of global musculature and observe that breathing is maintained normally.

1. Level of intensity 1 – 3 x 10 repetitions.

In supine position, slowly retract the chin against neck and go back to the start position. Repeat.

2. Level of intensity 2 – 3 x 30 seconds.

In sitting or standing position, slowly retract the chin against neck, hold with light pressure against the forehead and go back to the start position.

3. Level of intensity 3 – 3 x max seconds.

In supine position, slowly retract the shin against the neck, lift the head 1 cm above the bench maintaining the shin retracted.



1

2

3

2-Training of chest musculature (Push-ups plus)

- Purpose: to strengthen chest musculature and muscles around the scapula.
- Considerations: Minimize cervical and lumbar hyperlordosis and avoid elevation of scapula. Do a push-up with straight body, push the arms forwards once the up position is reached so that the scapula separates. Repeat.
 1. Level of intensity 1 – 3 x 10 repetitions against the wall or a bench
 2. Level of intensity 2 – 3 x 10 repetitions against the floor on the knees.
 3. Level of intensity 3 – 3 x 10 repetitions against the floor on the toes.



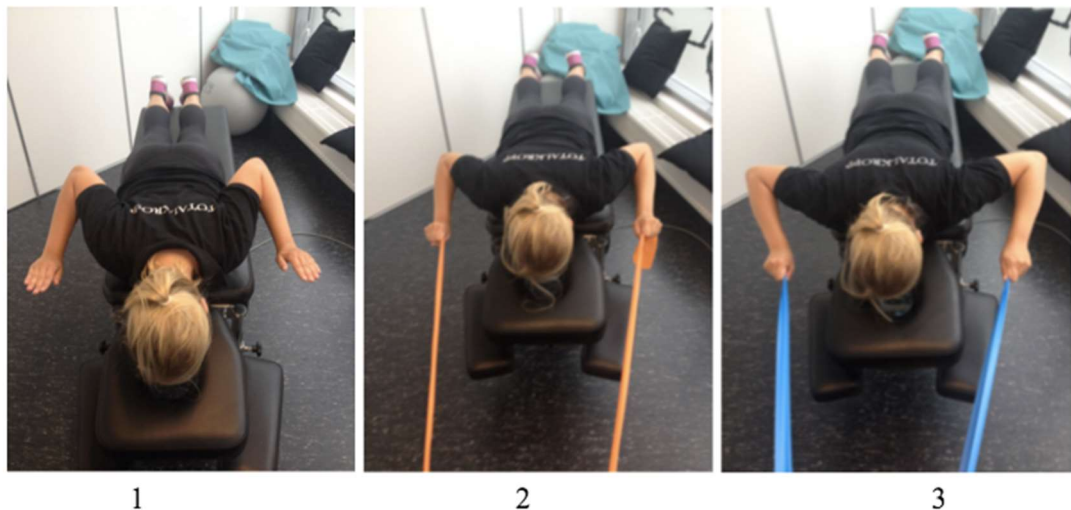
1

2

3

3-Training of scapula musculature (Lying pulldown)

- Purpose: to strengthen muscles around shoulders (M. serratus anterior, M. Trapezius pars ascendens) with simultaneous static control of the cervical musculature.
- Considerations: minimize cervical and lumbar hyperlordosis and avoid elevation of shoulders.
- In supine position retract the shin against the neck, lift the head 1 cm above the bench while maintaining the shin in the same position and hold. Drag the arms along the body (resembling a change from a “Y” position to a “W” position) and finish with contraction between the scapula. Repeat.
 1. Level of intensity 1 – 3 x 10 repetitions without rubber band.
 2. Level of intensity 2 – 3 x 10 repetitions with rubber band 1.
 3. Level of intensity 3 – 3 x 10 repetitions with rubber band 2.



4-Training of deep extensors of the neck

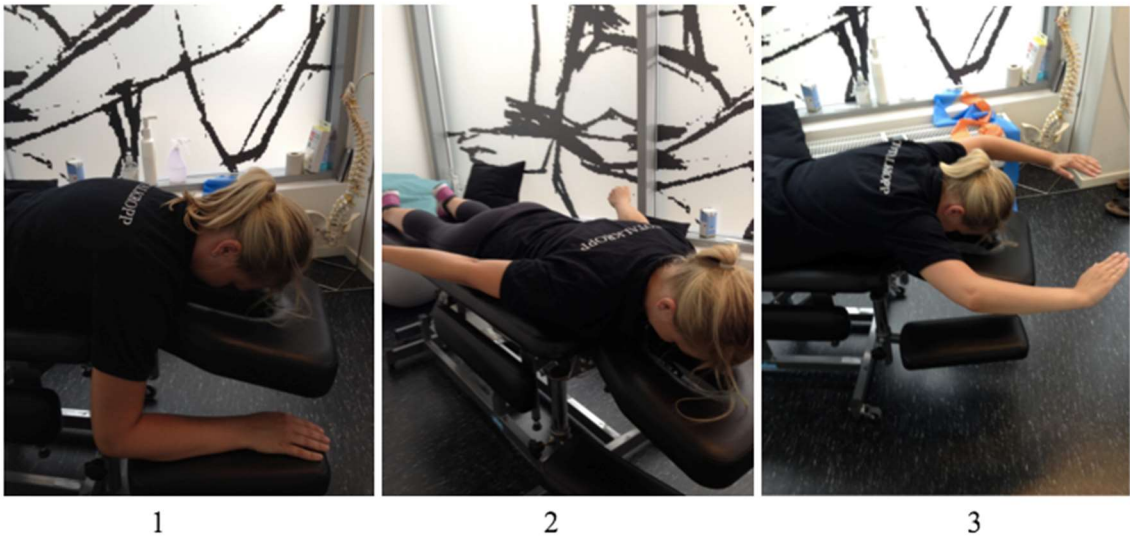
- Purpose: to strengthen deep extensors of the neck (M. Erector spinae).
- Considerations: high extension of the neck and compensation of global musculature.
 1. Level of intensity 1 – 3 x 1 minute.

In prone position, drag the shin against the neck, lift the head 1 cm above the bench while maintaining the same position and hold.
 2. Level of intensity 2 – 3 x 1 minute.

In prone position, hold the arms along the body, rotate the arms in and out with contraction of the area between scapula.

3. Level of intensity 3 – 3 x 1 minute.

In prone position, abduct and adduct the shoulder joint.



5-Training of the scapula musculature (scapulothoracic control exercise)

- Purpose: to strengthen muscles around shoulders (M. Trapezius pars descendens).
Alternative to participants with high levels of pain.
- Considerations: avoid elevation of scapula.
 1. Level of intensity 1 – 3 x 10 repetitions.
Standing/Sitting hold the hands behind the back, drag the shoulders back and downwards while contracting the area between scapulae. Repeat.
 2. Level of intensity 2 – 3 x 1 minute.
Lying on one side, flex and extend the free arm while maintaining the position of the scapulae.
 3. Level of intensity 3 – 3 x 1 minute.
In prone position, let the head rest, resemble a diamond shape with the arms and lift the hands by contracting the area between the scapulae.



6-Stretching of chest muscles

- Purpose: to decrease the tonus of the chest musculature (M. Pectoralis major).
- 15-20 seconds, 3 times each side. With flexed elbows against a wall, stretch out the chest musculature by rotating the body away from the arms.

7- Stretching – depressors of the shoulder.

- Purpose: to decrease the tonus in the depressors of the shoulder (M. Pectoralis minor).
- 15-20 seconds, 3 times each side. In a standing or supine position, elevate the shoulder and arm, rotate the body towards the opposite side and hold with flexed knees (if supine position).



8-Stretching – jaw musculature

- Purpose: to decrease the tonus in the jaw musculature (M. masseter, M. temporalis, Mm. pterygoidei).
- 15-20 seconds x 3 times. Open the jaw wide. Thereafter, strain the mouth by pressing the fingers against the upper and lower teeth.

9-Stretching – jaw musculature (Interoceptive neuromuscular facilitation)

- Purpose: to decrease the tonus in the jaw musculature (M. masseter, M. temporalis, Mm. pterygoidei).
- 3x10 repetitions. Place a fist under the shin. Open the jaw slowly with a light resistance with the fist. Hold for six seconds. Repeat.

10-Stretching – jaw musculature (Proprioceptive neuromuscular facilitation)

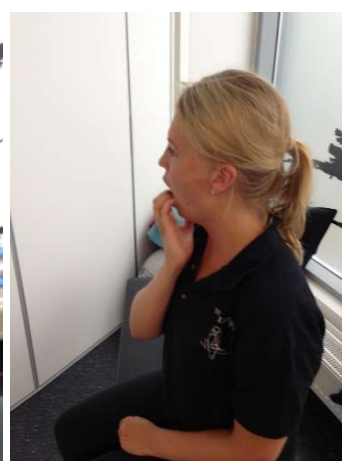
- Purpose: to decrease the tonus in the jaw musculature (M. masseter, M. temporalis, Mm. pterygoidei).
- 3x10 repetitions. Open the jaw, and try to close it while resisting the movement by dragging the lower portion of the jaw with the fingers placed on the lower teeth row.



8



9



10

4.3.3. Massage and exercise

A maximum of six sessions of therapies during the course of six weeks were recommended. The visit lasted 60 minutes and at least 25 minutes were dedicated to active treatment with strengthening and stretching exercises, followed by at least 25 minutes of deep tissue massage. The protocol was the same as described above.

4.3.4. Advice

A maximum of three visits were offered. Evidence-based advice was given based on scientific statements from SBU (Statens beredning för medicinsk och social utvärdering, *Swedish Agency for Health Technology Assessment and Assessment of Social Services*)¹⁰ and Cochrane^{34,35,65,66} consisting of the following elements:

- Adequate information on the condition and reassurance to the participant that the condition is not dangerous but a tolerable strain and that the most important aspect, according to previous experience and research, is to try to self-control their own pain by being active both socially and physically.
- Advice to the participant to be active and continue daily activities including work, if possible.
- Description of over-the-counter medications that could be used, if necessary, to relieve pain, mentioning that it is common to take, regularly, paracetamol at first, and then NSAIDs (observing that there are contraindications).
- Revision of which movements can be relevant according to standard recommendations (using the online resource Exor-Live®⁶⁷ for maximum three exercises) observing that this should not be as detailed and adjusted as the interventions in the exercise group.

Participants were classified into three different groups, as judged by the therapist:

1. Those who did not have physical activity as a habit (who were instructed on minimal exercises primarily oriented towards good circulation).
2. Those who had physical activity as a habit (adjustments were suggested to incorporate exercises to the training habit).
3. Those who were highly active (adjustments of the exercises to the training habit were suggested with focus on neck musculature).

Finally, a booklet was given with the different approaches to manage back and neck pain and informational facts about exercises.

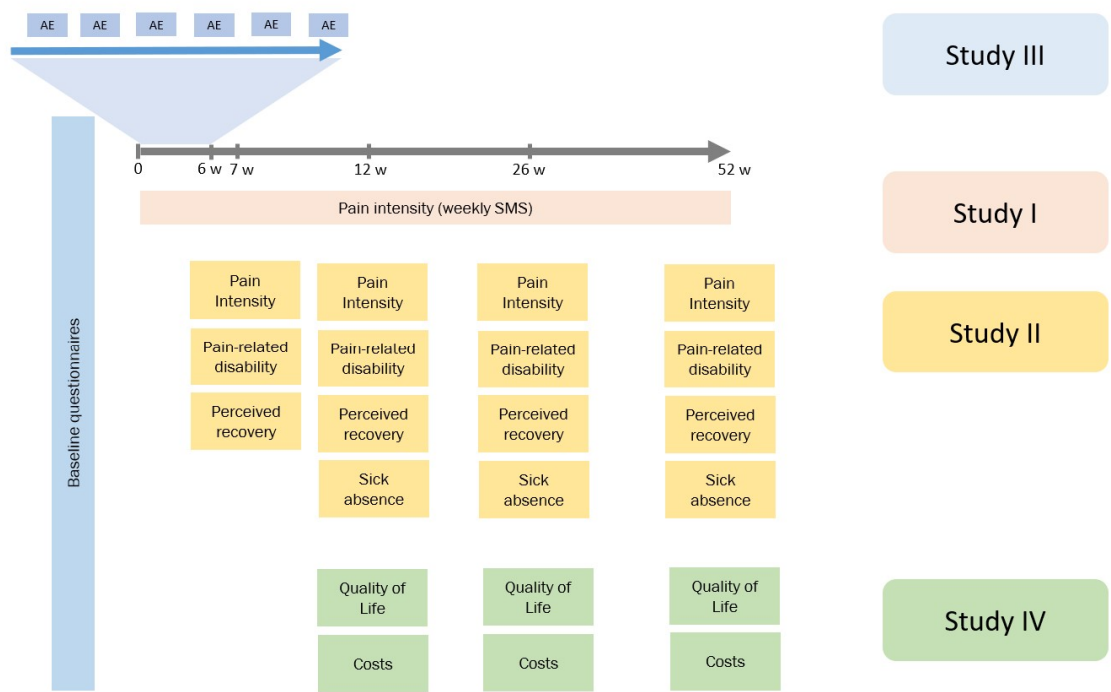
4.4. Follow-up and measurements

Follow-up questionnaires (see appendices) that contained questions to measure the effect of the therapies were distributed at 7 weeks from the study start, at 12 weeks (3 months), 26 weeks (6 months) and 52 weeks (one year) (Study II and IV). Several self-reported measurements were registered along the study (See Figure 1 and Table 1 for the questions asked in the questionnaire and that are relevant to this thesis).

Every time participants came back for a session of the assigned therapy (that is, starting from the second visit to the clinic), they were asked to fill out a questionnaire about adverse events that might have occurred during the first 24 hours post-treatment (Study III). At the end, they had filled out as many questionnaires as the number of therapy sessions that they had received. Those assigned to the advice to stay active group did not fill out any questionnaire regarding adverse events.

In addition to questionnaires, text messages were sent every week on Sunday afternoon for a year, asking about average pain intensity and pain-related disability during that week. Participants responded with a number from 0 to 10 (Study I).

Figure 1. Layout of the STONE trial.



AE: Adverse event.

Table 1. Selected variables included in the STONE trial. The full questionnaires in Swedish are attached at the end of this thesis.

Variable	Measurement	Classification	Measured at
Pain intensity	Three questions from Chronic Pain Grade Questionnaire ⁶⁸ were asked: 1. <i>How would you rate your pain on a 0-10 scale at the present time, that is right now, where 0 is “no pain” and 10 is “pain as bad as it could be”?</i> 2. <i>In the past 4 weeks, how intense was your worst pain rated on a 0-10 scale where 0 is “no pain” and 10 is “pain as bad as it could be”?</i> 3. <i>In the past 4 weeks, on average, how intense was your pain rated on a 0-10 scale, where 0 is “no pain” and 10 is “pain as bad as it could be”?</i>	The change in average pain (of the three questions) from baseline was dichotomized. Those with an improvement of at least 2 units in the numeric rating scale from 0 to 10, were classified as improved.	Baseline 7 weeks 12 weeks 26 weeks 52 weeks Weekly by SMS (question 3 only, asking for the past week)
Pain-related disability	Three questions from Chronic Pain Grade Questionnaire ⁶⁸ were asked: 1. <i>In the past 4 weeks, how much has this pain interfered with your daily activities rated on a 0-10 scale where 0 is “no interference” and 10 is “unable to carry on activities”?</i> 2. <i>In the past 4 weeks, how much has this pain changed your ability to take part in recreational, social and family activities where 0 is “no change” and 10 is “extreme change”?</i> 3. <i>In the past 4 weeks, how much has this pain changed your ability to work (including housework) where 0 is “no change” and 10 is “extreme change”?</i>	The change in average pain (of the three questions) from baseline was dichotomized. Those with an improvement of at least 1 unit in the numeric rating scale from 0 to 10, were classified as improved.	Baseline 7 weeks 12 weeks 26 weeks 52 weeks Weekly by SMS (question 3 only, asking for the past week)
Perceived recovery	A global perceived effect scale was used by asking: “How do you feel your symptoms in the neck have	Participants who reported to be significantly improved or completely pain-free (in	7 weeks

	<i>changed since you joined the study?</i> ⁶⁹	comparison to somewhat improved, no change, somewhat worsened or significantly worsened) were classified as recovered	12 weeks 26 weeks 52 weeks
Sickness absence	The following question was asked: <i>For how many workdays have you been at home/away from work or studies due to neck pain over the past [3-6 months depending on the follow-up]?</i>	Those who responded being away from work at least 1 day, were classified as being on sickness absence	12 weeks 26 weeks 52 weeks
Quality of life	We used the EQ-5D-3L questionnaire ⁷⁰	The answers from the questionnaire were transformed into a score with values from 0 to 1 to represent quality of life (1 being the optimal), using Swedish rates ⁷¹ .	Baseline 12 weeks 26 weeks 52 weeks
Expectations on the treatment	The following question was asked: <i>What impact do you think the assigned treatment will have on your recovery?</i>	A NRS scale from 0 to 10 was used, 0 meaning “no impact at all” and 10 meaning “crucial impact”	Baseline
Expectations on full recovery	The following question was asked: <i>According to you, how likely is it that you will be completely symptom-free in your neck within 7 weeks?</i>	A NRS scale from 0 to 10 was used, 0 meaning “not likely” and 10 meaning “very likely”.	Baseline
Occupation	Participants were asked to write down their main current occupation.	We used the Swedish standard classification of occupations ⁷² and built four groups: managerial or high university degree, university level, service and technical, and students and retired.	Baseline
Job demands	We used the Job Content Questionnaire ⁷³ 1. <i>Do you have enough time to complete your work duties?</i> 2. <i>Do you experience conflicting demands?</i>	Depending on the answer to those two questions, participants are classified as having a low, moderate or high demand job.	Baseline 52 weeks
Job control	We used the Job Content Questionnaire ⁷³	Depending on the answer to those two questions, participants are classified as	Baseline 52 weeks

	<ol style="list-style-type: none"> 1. <i>Do you have freedom to decide what gets done at your work?</i> 2. <i>Do you have freedom to decide how your work should be completed?</i> 	having a low, moderate or high job control.	
Smoking habit	<p>We asked the following question:</p> <p>Do you smoke daily?</p>	The answer alternatives were Yes or No.	Baseline
Body mass index	We asked the participants to report their weight in kilograms at the moment of the interview and their height in centimeters.	We used the formula: $\text{Weight (in Kg)} / \text{Height}^2 \text{ (in m)}^{74}$ to calculate body mass index.	Baseline
Depressive symptoms	Seven questions (those enquiring about depressive symptoms) from the Hospital Anxiety and Depression scale (HADS) were used. ⁷⁵	We assigned a value from 0 to 3 to each of the seven questions. Those who had at least 9 points were classified as “with depressive symptoms”. ⁷⁵	Baseline 52 weeks
Visits to healthcare providers not part of the trial	<p>We asked whether participants had visited (and if yes, how many times) each of the following providers:</p> <ol style="list-style-type: none"> 1. Physiotherapist 2. Naprapath 3. Chiropractor 4. Osteopath 5. Masseur 6. Medical doctor 7. Other* 	If they answered yes to any of the items, a cost was assigned based on the market prices in Stockholm for the years 2017/2018	Baseline 12 weeks 26 weeks 52 weeks
Diagnostic aids used	We asked whether participants had any checkups in the form of X-rays or similar. If they answered yes, we asked them to describe which diagnostic aid and how many times they received them.	If they answered yes, a cost was assigned based on the market prices in Stockholm, which we obtained by calling a sample (by convenience) of providers in the city during 2017/2018.	Baseline 12 weeks 26 weeks 52 weeks
Use of allopathic and homeopathic preparations	<p>Questions were asked about three different types of preparations:</p> <ol style="list-style-type: none"> 1. Alternative medicine 2. Over the counter medications 3. Prescribed medications 	<p>If yes, we asked them to specify which preparation and how often they took it: “sometimes” (which we assumed to be twice per week) and “daily”.</p> <p>A cost was assigned based on prices from the Dental and Pharmaceutical Benefits Agency in Sweden (TLV)^x</p>	Baseline 12 weeks 26 weeks 52 weeks

Occurrence of adverse events within the 24 hours post therapy	<p>We used three questions to</p> <ol style="list-style-type: none"> 1) <i>Have you experienced [type of adverse event] as a direct result of treatment/training received?</i> 2) <i>If yes, How long did the reaction last?</i> 3) <i>How much did it bother you? (In a numeric rating scale from zero to 10).</i> <p>These questions were repeated for seven different types of AE: (1) tiredness, (2) sore muscles, (3) stiffness, (4) increased pain, (5) dizziness, (6) headache, (7) nausea and an additional question on (8) other types, which participants who answered yes were asked to name.</p> <p>Additionally, we asked them to rate from 0 to 10, how bothersome the adverse event had been for their daily activities.</p>	<p>We classified each of the adverse events as slightly bothersome, moderately bothersome and highly bothersome.</p>	Weeks 2-7
---------------------------------------------------------------	------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------	----------------------------------------------------------------------------------------------------------------------	-----------

*For example: yoga instructor, personal trainer, psychologist, homeopathic medicine clinics.

4.5. Analyses

4.5.1. Study I

With relatively recently developed methods, it is possible to describe the course of a disease to find clusters of similar individuals based on the trajectories of their symptoms.⁷⁶ This is valuable for increasing the understanding of the natural history of the condition. It also allows, in a second step, the identification of variables associated with certain trajectories.⁷⁷ For this purpose, latent class growth analysis and latent class growth mixture modeling are the most up-to-date and popular methods.⁷⁸ The difference is that the latter assumes variations (heterogeneity) within the generated clusters, while the former does not.⁷⁹

In this study, we used information from weekly reports on pain intensity over one year. Participants answered with a number from 0 to 10 how much pain they had experienced during that week. With that information, we created a database for all the individuals, in which every person had up to 52 values (corresponding to the 52 weeks of follow-up). We created a line graph (a line over time) for each participant and thereafter placed all the

participants' line graphs in one single plot. Using the package for LCMM (latent class mixture modeling) of the statistical program "R"⁸⁰, clusters of participants were created based on similarities in the shape of their individual line graphs over time. The number of clusters was determined by the Bayesian Information Criterion.

After these clusters were formed, we observed the average curve of pain intensity (termed 'trajectory') for each of the clusters and judged them as favorable or unfavorable. A favorable trajectory was considered when there was a decrease in pain intensity over time, followed by stable values. An unfavorable trajectory was considered when there were no clear decreases in pain intensity, or when there were big or small fluctuations over time around the area corresponding to high pain intensity.

Once we had identified which trajectories were favorable or unfavorable, we looked at certain baseline characteristics of the participants that belonged to each one of those two groups (favorable or unfavorable) and compared them to each other. These characteristics were sex, age, psychological distress, pain intensity at baseline, onset of neck pain and duration of neck pain.

4.5.2. Study II

We asked several questions at 7, 12, 26- and 52-weeks of follow-up using questionnaires. Similar to what we did with the information from the text messages, we built a database containing each participant's answer to each item of the questionnaire. We followed an intention to treat approach, meaning that all the comparisons were done among the four original groups as the research team assigned them by the randomization procedure irrespective of their adherence to treatment. The four treatment groups were: (1) massage alone, (2) exercises alone, (3) combined massage and exercises, or (4) advice. We considered advice as the reference, so all the comparisons were made against that group.

To assess the effectiveness of the therapies we considered four parameters: two primary outcomes and two secondary outcomes. The primary outcomes were: (a) change from baseline in pain intensity (a decrease of at least 2/10 points was considered a successful response: minimal clinically important improvement in pain intensity), and (b) change from baseline in pain-related disability (a decrease of at least 1/10 points was considered a successful response: minimal clinically important improvement in pain-related disability). The secondary outcomes were: (a) self-perceived recovery (those who reported being "completely pain free" or "significantly improved" were considered a successful case), and

(b) sickness absence (those who reported being off work due to neck pain at least one day were considered to be in sickness absence).

Given that we measured the same items on repeated occasions (at baseline, and at 7, 12, 26 and 52 weeks) we used the generalized estimating equations method⁷⁹ to adjust for the correlations between the answers within each individual (since people are likely to think about their previous answers when asked the same question again rather than answer totally independently). We reported the results as Risk Ratios (RR) with 95% confidence intervals (95% CI), in relation to the reference group ‘advice’.

When we present the results, the RR refer to the average effect of the treatment in the whole group. We also calculated the “number needed to treat” (NNT) (as the inverse of the difference between each group and advice in the proportions of participants achieving a certain outcome) which refers to how many people need to receive a certain therapy to achieve one successful case of recovery: the larger the number, the lower the effect.

4.5.3. Study III

We calculated the occurrence of adverse events (AE) for participants in three of the intervention arms: (1) massage alone, (2) exercises alone, and (3) combined massage and exercises by dividing the number of participants reporting a given adverse event by the total number of participants in each intervention arm. Based on the question *How much did it bother you? (In a numeric rating scale from zero to 10)*, each of the adverse events was classified as follows: none or mild (0-3/10), moderate (4-6/10) or high (7-10/10) degree of bothersomeness. In addition, we measured the number of times that each type of AE was reported and divided it by the time all persons were followed-up (incidence rate). Finally, a ratio between the interventions was calculated (incidence rate ratio).

We compared benefits versus harms among participants who answered that a certain adverse event bothered them to a degree of at least 7/10. To do this, first we measured ‘the benefit’ with the outcome perceived recovery^{81,82} at seven weeks (benefits) by asking: “*How do you feel your symptoms in the neck have changed since you joined the study*”. A favorable perceived recovery was defined as those reporting their pain being significantly improved or completely pain-free (in comparison to somewhat improved, no change, somewhat worsened or significantly worsened). Exercise showed a lower proportion of participants achieving perceived recovery (23%) than massage (41%) or combined therapy (38%). Therefore, we considered it as the control or reference group for the first set of comparisons; we used

combined therapy as the reference for the comparison between massage and combined therapy.

We used the same methods as in Study II to calculate the number needed to harm (number needed to treat in Study II), but they were interpreted differently here, since the outcome is the harm (adverse event) caused by the therapy, rather than the benefit. Larger numbers are good, because it means that many participants need to be treated for an adverse event to be observed. To facilitate the interpretation of the results, when any of the therapies showed both better effects and less adverse events, we reported “< 0” instead of a quantity. Finally, we compared the benefits and the harms, and calculated the likelihood of being helped versus harmed by dividing the number needed to harm by the number needed to treat. For that measure, large numbers are good, since it means that many participants will achieve benefits for one participant experiencing an adverse event.

4.5.4. Study IV

Neck pain is a costly condition for the society because it leads to: (1) direct costs due to people seeking care with doctors, physiotherapists and other providers (which in Sweden is paid by the residents through taxes); and (2) sick leave due to inability to work (which is also paid through taxes). For example, investing more money from Swedish taxes in treating people – with for example, neck pain – would leave less resources for education, infrastructure or environmental issues. Therefore, we performed the analyses considering a societal perspective, meaning that we assume that the costs of the studied therapies are paid by the whole society. In addition, we assume that the benefits achieved with the therapies included in this trial will eventually increase the quality of life of people with neck pain, making them capable of working without major impairment and benefit the society.

Similar to Study II, we also followed an intention to treat approach here. Since we measured the effects of the therapies for up to 52 weeks (one year), we did not adjust for inflation or loss of value as is done when the assessment is conducted along more than one year. The measure we used to assess the benefit generated from the therapies was quality-adjusted life years. One quality-adjusted life year is equal to one person living in perfect health during one year. We calculated this based on the answers to the EQ-5D questionnaire, which was included in the follow-up assessments.

For each of the four therapies that we compared in the STONE trial, we calculated the amount of quality-adjusted life years. Thereafter, we ranked them from the highest to the

lowest and looked at the costs associated with each one of the therapies. This was done to discard therapies that did not generate as many gains in quality-adjusted life years and were very costly. If a therapy resulted in larger quality-adjusted life years but was more expensive than another one, then an additional comparison was made, using a cost-effectiveness analysis.

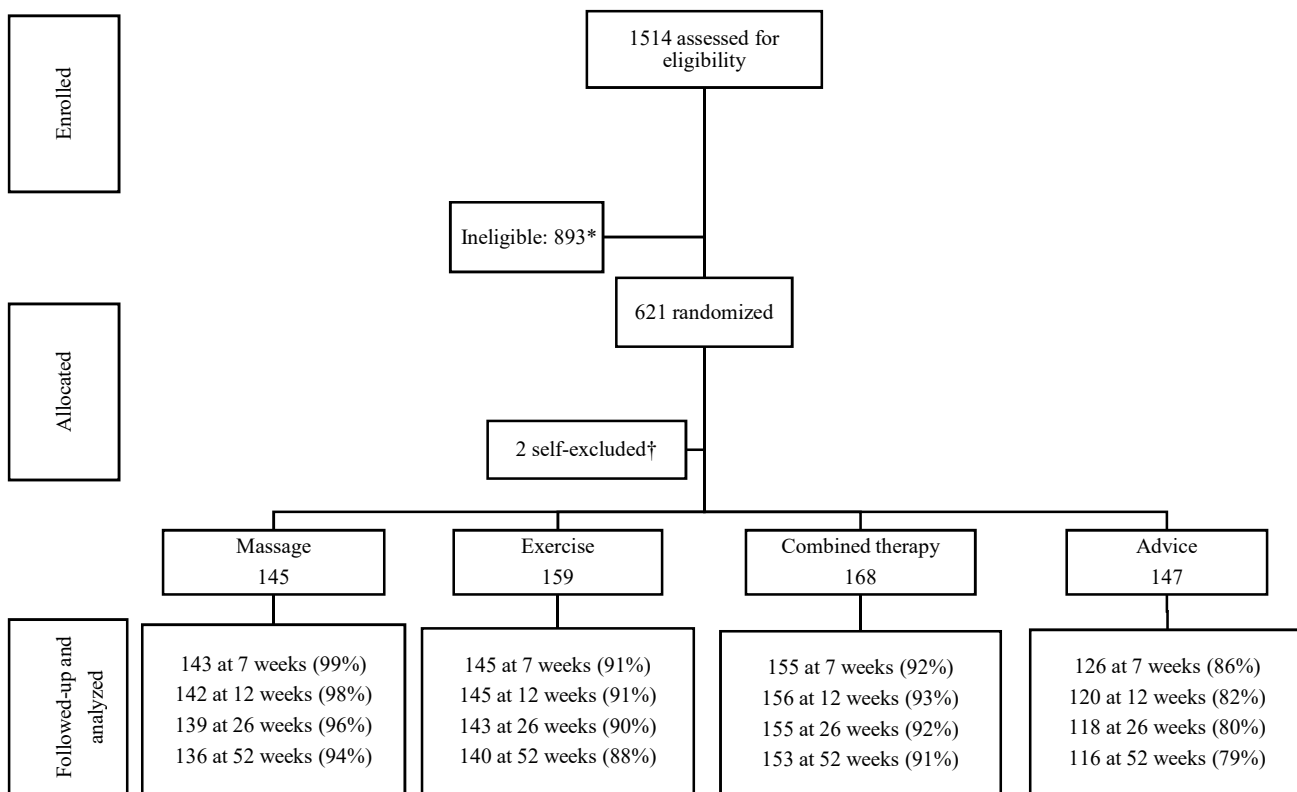
In the cost-effectiveness analysis, two options were compared. Typically, both are effective, but one is more effective than the other (effectiveness is measured with the amount of quality-adjusted life years) and, usually, the more effective one is more expensive. The difference in effectiveness between the two was calculated, as well as the difference in cost. Following this, such differences were compared in an index called the incremental cost-effectiveness ratio, which reveals how much it costs to get those extra quality-adjusted life years by using the most expensive treatment instead of the less expensive one. We replicated the analysis ('bootstrapped') 5000 times to account for results due to chance and plotted the results in a graph. Last, we created a cost-effective acceptability curve, which shows how likely it would be for a certain therapy to be considered worth paying for.

5 RESULTS

5.1. Inclusion of participants

More than 1500 people were interested in being part of the STONE trial. Eventually, 621 reached the point of being randomized to one of the therapies. The most common reason for not being eligible was unwillingness to complete the treatment and/or the follow-ups for one year. Other reasons (see full list below Figure 2) were not having pain in the neck area or it having lasted for less than a month.

Figure 2. Flow of participants in the Stockholm Neck Trial.



*Description of ineligible subjects in numbers: 1) Not willing to complete the trial: 520; specific diagnosis: 155; no neck pain: 24; pain < 30 days: 25; ineligible age: 14; not fluent in Swedish: 9; no smartphone: 2; mild symptoms: 22; previously enrolled: 1; treatment in the past 30 days: 74; specific training for neck pain: 7; cancer: 15; red flags: 22; contraindication: 3. †Quit and requested to delete all their information from the study. One belonged to exercise and one to combined therapy.

5.2. Population characteristics

We included 619 participants in our analyses. On average, they were 47 years old and most of them were women (Table 2). The majority had more than 12 years of education and worked in occupations that are managerial, require a university degree, are related to administration or are client-related. Most of the participants had neck pain that lasted one year or longer. Typically, the neck pain started gradually, rather than suddenly. On average, participants had a pain intensity of 6/10 and a pain-related disability of more than 4/10 when they were enrolled in the study.

5.3. Study I

Most participants responded to the text messages that we sent every week: 90% of the text messages sent were answered, which was a very good response rate. As presented in the methods section, we created groups of participants who shared similar shapes (trajectories) in the course of their pain over one year. With the statistical program, we identified six different clusters of participants (also called clusters).

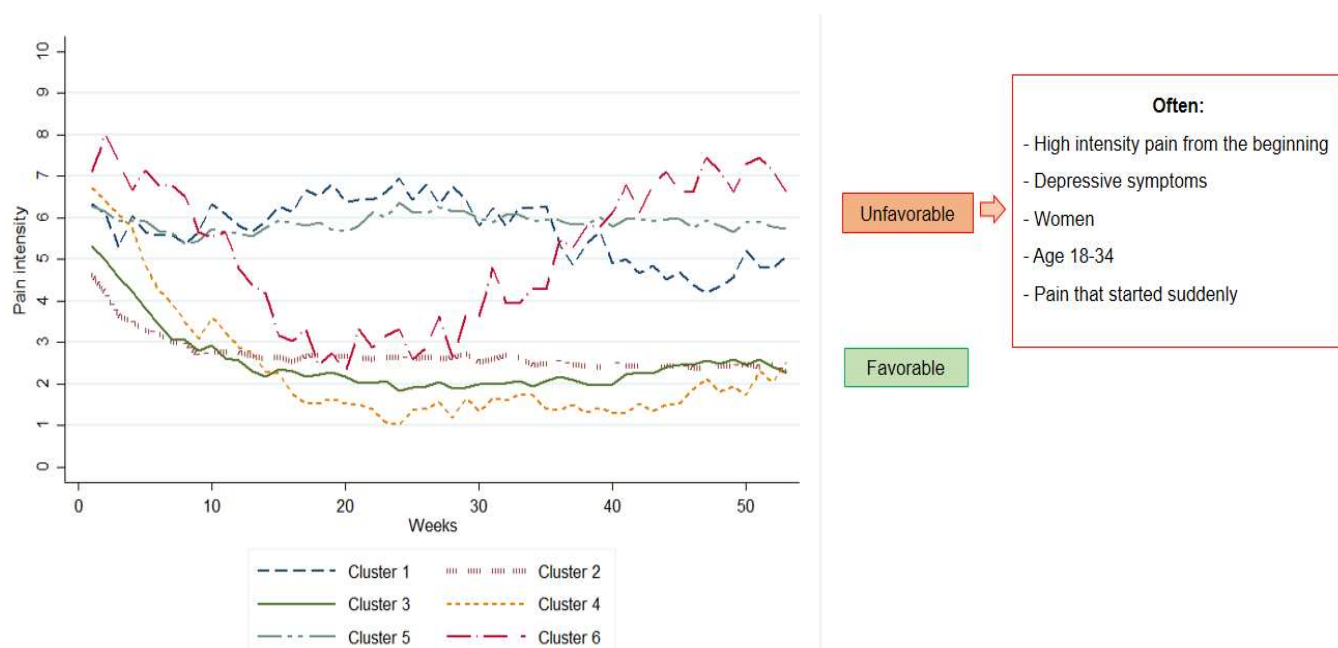
Figure 3 shows the six identified clusters of trajectories. The most common cluster was number 2, to which 42% of the participants belong. This one was considered a favorable cluster, because, on average, participants reported a decrease in pain intensity during the first weeks of the follow-up and continued reporting low pain-intensity. Clusters 3 and 4 were also considered favorable trajectories.

On the other hand, we observed that one out of four participants had unfavorable courses of pain (Figure 3). The most common unfavorable cluster was number 5 (22% of the total participants). People in this cluster reported almost no changes in the pain intensity, which persisted around 6/10. Finally, participants in the unfavorable clusters (those in cluster 5, 1 and 6) were more often individuals who had depressive symptoms at baseline, higher pain intensity at baseline, aged 18-34, women and those with neck pain that started suddenly.

Table 2. Baseline characteristics of the study participants by treatment group.

	Massage n= 145		Exercise n= 159		Combined therapy n= 168		Advice n= 147	
Age, mean (SD)		48(14)		47(14)		45(14)		46(13)
Sex, female	97	67%	112	70%	119	71%	98	67%
Education								
12 years or less	43	30%	55	35%	65	39%	54	37%
More than 12 years	102	70%	104	65%	103	61%	93	63%
Occupation category⁷²								
Managerial or graduate university degree	56	39%	61	39%	75	45%	71	48%
University degree, administration and client-oriented	41	28%	53	33%	33	20%	34	23%
Service, care, sales, construction, transportation or short education	23	16%	26	16%	33	20%	27	19%
Student/retired/other	25	17%	19	12%	25	15%	15	10%
Duration of neck pain								
1-3 months	20	14%	34	21%	33	20%	25	17%
4-6 months	15	10%	20	13%	27	16%	23	16%
7-12 months	18	12%	17	11%	12	7%	11	7%
12+ months	92	64%	88	55%	96	57%	88	60%
Characteristics of pain onset								
Sudden	32	22%	30	19%	35	21%	34	23%
Gradual	89	61%	115	72%	111	66%	91	62%
Unsure	24	17%	14	9%	22	13%	22	15%
Pain intensity at baseline, mean (SD)		5.9(1.3)		6.1(1.3)		6.1(1.5)		5.8(1.5)
Pain-related disability at baseline, mean (SD)		4.4(2.0)		4.2(1.8)		4.3(1.7)		4.3(1.7)
Previous episodes of NP	67	46%	74	47%	90	54%	75	51%

Figure 3. Mean pain intensity over time by clusters generated with the latent class mixture modeling analysis.



5.4. Study II

As described in the methods section, we used four different parameters to evaluate the effectiveness of the therapies offered in the STONE trial. Two of those parameters were considered the “primary outcomes”: minimal clinically important improvement in pain intensity and minimal clinically important improvement in pain-related disability. The other two were “secondary outcomes”: self-perceived recovery and sickness absence. We compared the proportion of persons in each of the assigned groups that reached each of the four endpoints at 7, 12, 26, and 52 weeks and calculated RR (Table 3).

5.4.1. Primary outcomes

In most of the cells in Table 3, we observed risk ratios (RR) very close to “1” and confidence intervals indicating that massage alone, exercises alone or combined massage plus exercise are equally effective as advice to stay active in reducing pain-intensity or pain-related disability. There are a few exceptions. Massage alone seemed to be slightly more effective than advice at reducing pain intensity at 7 weeks and 26 weeks. Exercises alone seemed to be slightly more effective than advice at reducing pain intensity at 26 weeks. The combined therapy seemed to be slightly more effective than advice at reducing pain intensity at 7 weeks and 12 weeks.

5.4.2. Secondary outcomes

Massage alone and the combined therapy was more effective than advice at all follow-ups. Exercise alone was also more effective than advice during the follow-ups, but not so much at one year. On the other hand, receiving massage alone, exercise alone and the combined therapy seemed to be associated with taking at least one day off work due to neck pain to a greater extent than those in the advice group at 26 weeks. None of the therapies were more or less effective than advice at preventing taking days off work at 12 weeks or 52 weeks.

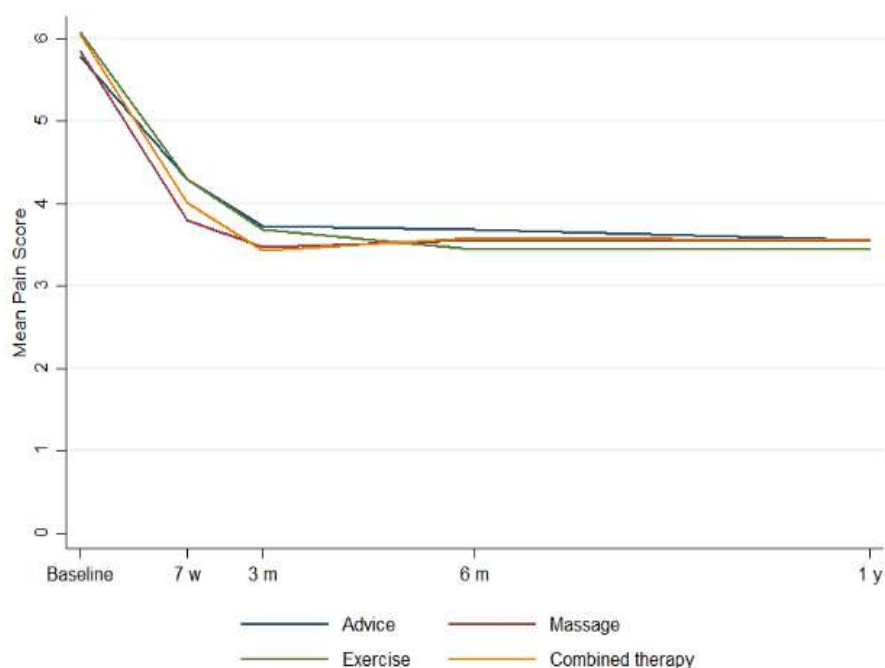
Table 3. Risk ratios (RR) and 95% Confidence Intervals (95% CI) of having the primary and secondary outcomes at four time points over one-year follow-up in the index groups compared to the reference group advice to stay active.

	Massage		Exercise		Combined therapy	
	RR	95% CI	RR	95% CI	RR	95% CI
PRIMARY OUTCOMES						
Minimal clinical important improvement of pain						
7 weeks	1.36	1.04-1.77	1.14	0.86-1.51	1.39	1.08-1.81
12 weeks	1.09	0.85-1.39	1.00	0.78-1.29	1.28	1.02-1.60
26 weeks	1.23	0.97-1.56	1.31	1.04-1.65	1.15	0.90-1.46
52 weeks	1.03	0.83-1.29	1.11	0.90-1.37	1.10	0.89-1.35
Minimal clinical important improvement of pain-related disability						
7 weeks	1.11	0.97-1.27	1.00	0.86-1.15	1.08	0.95-1.23
12 weeks	0.96	0.85-1.10	0.94	0.83-1.07	1.04	0.93-1.17
26 weeks	1.02	0.89-1.18	1.03	0.90-1.18	1.08	0.94-1.23
52 weeks	0.98	0.86-1.11	1.03	0.92-1.17	1.06	0.94-1.19
SECONDARY OUTCOMES						
Perceived recovery						
7 weeks	3.29	2.00-5.42	1.66	0.95-2.89	3.01	1.82-4.96
12 weeks	2.27	1.44-3.57	1.61	1.00-2.61	2.01	1.27-3.18
26 weeks	1.98	1.27-3.09	1.74	1.10-2.74	2.12	1.38-3.27
52 weeks	1.74	1.13-2.67	1.33	0.84-2.09	1.99	1.32-3.00
Sickness absence^a						
7 weeks	-	-	-	-	-	-
12 weeks	0.85	0.46-1.58	1.04	0.59-1.84	1.14	0.65-1.97
26 weeks	1.37	0.64-2.95	1.71	0.83-3.51	1.98	0.99-3.96
52 weeks	1.08	0.65-1.81	1.07	0.64-1.78	1.03	0.62-1.70

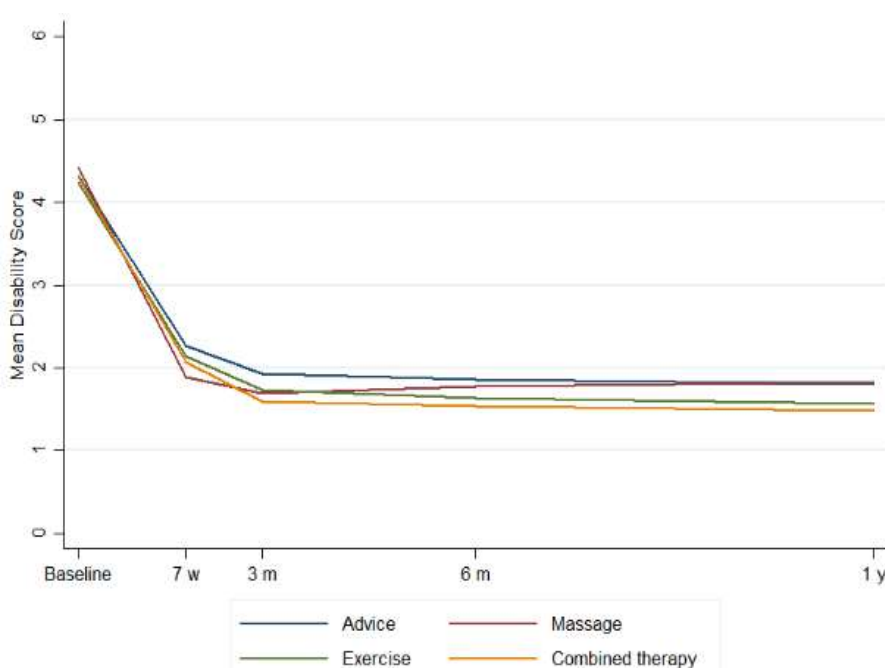
^aInformation on sickness absence was not collected at the 7 weeks questionnaire.

The figures below (Figure 4A and 4B) show the average pain for each of the four groups during the study period. No clear differences between the interventions were observed, either in pain intensity or in pain-related disability. However, there was a small gap between the lines of the massage and the massage plus exercise groups, and the lines of the advice and exercise groups at the start of the follow-up.

Figure 4. A) Mean pain intensity at baseline and follow-ups. B) Mean pain related disability at baseline and follow-up.



4A.



4B.

5.5. Study III

In total, 87% of the participants reported at least one adverse event at least once as result of the therapies provided in the STONE trial. In the methods section we described that we inquired about the bothersomeness of the adverse events. Participants who answered that a certain adverse event bothered them to a degree of at least 7/10 were included in further analyses. Of the participants 35% reported at least one adverse event of bothersomeness level equal or greater than 7/10, at least once, as a result of receiving the therapies provided in the STONE trial.

Results are presented in Table 4. There are two main sections in this table. The first section (columns 2-4) shows the number (“n”) and the percentage (“%”) of participants who reported adverse events that were highly bothersome (at least 7/10). The rest of the columns (5-13) are based on these values.

The second section (columns 5-13) shows different elements:

- (1) The difference in the percentage between two treatments, for example in the first line, we see that exercises led to 6.1% of the participants to experience the adverse event “tiredness” and massage led to 12.5% of the participants to experience that adverse event. Therefore, the difference is 6.4% ($12.5\% - 6.1\% = 6.4\%$).
- (2) The range (confidence interval) of the difference as explained above. Here, we say that if the range (confidence interval) includes “0” it is more likely (compared to ranges that do not include “0”) that treatment X, Y or Z and the reference treatment are equally harmful (harmful because in this case, it is an undesired effect, here called adverse events) or that there are probably no differences.
- (3) Number needed to harm (NNH). This is the number of persons receiving a treatment that will experience an undesired effect (adverse event) at least once. The higher the number, the better. For example, a NNH of 100 means that 100 persons need to be treated for one person to experience an adverse event. An NNH of 2 means that for every 2 persons treated, one will experience an adverse event. Negative values (presented as “<0”) indicate that a treatment is associated with less adverse events than the reference treatment.
- (4) Likelihood of being helped versus harmed (LHH). This is a comparison of NNH and NNT (which was described in Study II). It indicates the numbers of persons that benefit

from the treatment for every person that experiences an undesired effect at least once. The higher the number, the better. For example a LHH of 50 means that 50 persons will benefit for every person that gets one adverse event. A LHH of 8 means that 8 persons will benefit for every person that gets one adverse event. The NNT used to calculate the LHH is shown in the title row.

By looking at the range of the difference in percentages, we observed that the risk of being harmed was virtually the same for massage alone, exercise alone or combined therapy. None of the adverse events resulted in hospitalizations, emergency visits, death or any other serious outcome.

Table 4. Benefit-harm profile for highly bothersome AE in participants attending at least three sessions of therapy.

Adverse	ET	MT	CT	MT vs. ET* (NNT= 6)			CT vs. ET* (NNT= 7)			MT vs. CT* (NNT= 28)		
Event	n= 133	n= 141	n= 152									
	n (%)	n (%)	n (%)	RD (95% CI)	NNH	LHH	RD (95% CI)	NNH	LHH	RD (95% CI)	NNH	LHH
Tiredness	8 (6.1)	17 (12.5)	12 (8.0)	6.4 (-0.5 to 13.3)	16	3	1.8 (-4.1 to 7.8)	55	8	4.6 (-2.5 to 11.6)	22	1
Soreness	23 (17.6)	18 (13.2)	28 (18.5)	-4.3 (-13.0 to 4.3)	< 0	< 0	1.0 (-8.0 to 10.0)	102	15	-5.3 (- 13.7 to 3.1)	< 0	< 0
Stiffness	22 (16.8)	9 (6.6)	19 (12.6)	-10.1 (-17.8 to -2.5)	< 0	< 0	-4.2 (-12.5 to 4.1)	< 0	< 0	-6.0 (-12.7 to 0.8)	< 0	< 0
Increased pain	29 (22.1)	27 (19.9)	34 (22.5)	-2.3 (-12.1 to 7.5)	< 0	< 0	0.4 (-9.3 to 10.1)	264	39	2.7 (-12.1 to 6.8)	38	2
Headache	6 (4.6)	8 (5.9)	8 (5.3)	1.3 (-4.0 to 6.6)	77	15	0.7 (-4.3 to 5.8)	139	21	0.6 (-4.7 to 5.9)	173	7
Dizziness	22 (16.8)	26 (19.1)	35 (23.2)	2.3 (-6.9 to 11.5)	57	8	6.3 (-2.9 to 15.7)	16	3	-4.1 (-13.5 to 5.4)	< 0	< 0
Nausea	5 (3.8)	4 (2.9)	6 (4.0)	-0.9 (-5.2 to 3.5)	< 0	< 0	0.2 (-4.4 to 4.7)	639	94	-1.0 (-5.3 to 3.2)	< 0	< 0
Other	6 (4.6)	11 (8.1)	12 (8.0)	3.5 (-2.3 to 9.3)	29	6	3.4 (-2.2 to 9.0)	30	5	0.1 (-6.2 to 6.4)	715	27

ET: exercise therapy. MT: massage therapy. CT: combined therapy. AE: adverse event. RD: risk difference. *Denotes the reference group.

5.6. Study IV

We chose quality-adjusted life years to measure ‘benefits’. We observed that exercises alone and advice resulted in the highest benefit (Table 5). However, the differences were in fact, very small. Exercises alone and advice were also the least costly. Given that massage alone and the combined therapy were the least beneficial in terms of quality-adjusted life years and the costliest ones, we excluded them from further analyses.

Table 5. Cost-consequence analysis of the interventions in the STONE trial.

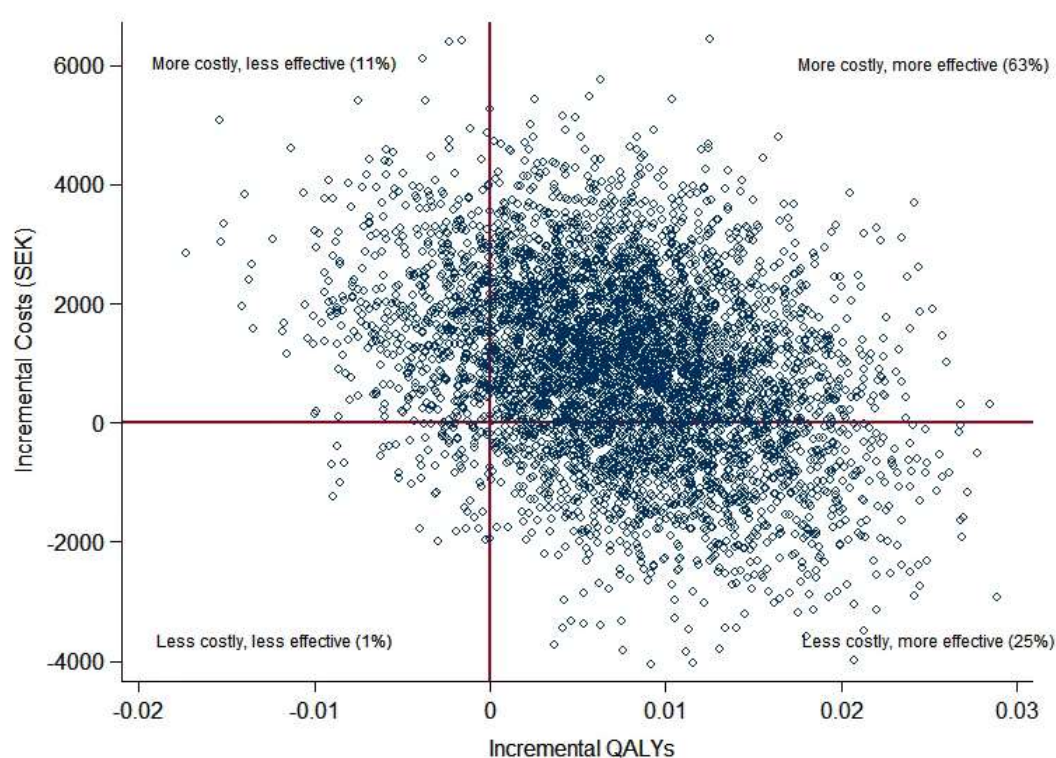
Intervention	QALY	Cost*	Notes
Exercises	0.8930	11,781 SEK (1186 EUR)	More costly and more effective than advice to stay active Less costly and more effective than combined therapy Less costly and more effective than massage therapy
Advice to stay active	0.8844	10,265 SEK (1033 EUR)	Less costly and less effective than exercises Less costly and more effective than combined therapy Less costly and more effective than massage therapy
Combined therapy	0.8840	14,663 SEK (1476 EUR)	More costly and less effective than exercises More costly and less effective than advice to stay active Less costly and more effective than massage therapy
Massage therapy	0.8817	19,669 SEK (1979 EUR)	More costly and less effective than exercises More costly and less effective than advice to stay active More costly and less effective than combined therapy

*After adjusting for the high-cost threshold.

The cost-effectiveness analysis was repeated 5000 times to account for uncertainty around the estimated ratio between QALYs and costs (Figure 5). The reference treatment was advice. In 25% of the 5000 repetitions, exercises were considered cheaper and more effective than

advice. In 11%, they were considered more costly and less effective. In 63%, exercises were considered more costly but also more effective. We found that for an individual with neck pain to gain one year of perfect health (by treating them with exercise instead of advice), the cost to Swedish taxpayers would be 175,295 SEK (17,640 EUR). To have a reference, Swedish society considers 500,000 SEK (50,315 EUR) to be the limit for what it can consider affordable.

Figure 5. Cost-effectiveness plane between exercises and advice to stay active.



6 DISCUSSION

6.1 Main findings

The STONE trial was a study of participants with non-specific subacute or chronic pain. We confirmed the benign nature of persistent chronic neck pain by observing that most individuals improved in terms of pain intensity over one-year follow-up. However, we also identified that a quarter of them reported high pain intensity constantly, with small, or with large, fluctuations. As expected, based on the existent literature on prognostic factors for chronic neck pain⁸, female sex and depressive symptoms, in addition to baseline pain intensity, were the factors more strongly associated with unfavorable courses of neck pain.

We found that compared to advice to stay active, massage and combined therapy resulted in a slightly better effect at achieving minimal clinically important improvement in pain intensity in the short term but not in the long term. Exercise was slightly better in the mid-term (six months). There were no differences in the effects on minimal clinically important improvement in pain related disability among therapies. We found that massage, exercises and combined therapy resulted in better perceived recovery than advice at all follow-ups, which we attributed to the interventions targeting other dimensions of the pain experience. Mostly, there were no differences in the effects on sickness absence. However, exercise and combined therapy appeared to be associated with a higher risk for sickness absence than advice in the mid-term (at six months).

Adverse events were common but not serious. The most common adverse events were tiredness, muscle soreness, stiffness and increased pain. Less common adverse events were dizziness, headache and nausea. Massage resulted in more highly bothersome adverse events compared to exercise. However, between-group differences in the incidence of these adverse events were not considerable. We did not study occurrence or the impact of adverse events beyond seven weeks follow-up.

Costs were higher for combined therapy and for massage than for advice (the reference group). Although differences in gains of health-related quality of life were very similar between the four groups, combined therapy and massage had the smallest gains. Exercises were more costly than advice but resulted in higher gains of health-related quality of life. For this reason, exercise and advice were compared in terms of costs per gains of health-related

quality of life. It was found that exercise would have above a 60% probability of being classified as cost-effective.

When it comes to improvement of pain intensity, the literature shows mixed results. However, a great variation depends on which control group was used to evaluate the intervention. For instance, an intervention is more likely to show positive results if it is compared to passive interventions such as a booklet⁵⁰, sham interventions,⁸³ recommendations of general physical activity or specific exercises^{84,85}. Combinations of therapies have also shown better results at reducing pain intensity.⁸⁶

6.2 Methodological considerations

6.2.1. Describing the disease: trajectories of neck pain

To achieve our aim of advancing our knowledge of the course of neck pain, we chose to analyze our data by identifying different trajectories over one year using a latent class mixture model. There is debate on the varying number of clusters resulting from such analysis, which is determined by the data itself and can vary depending on the chosen model.⁷⁸ For instance, the larger the sample size, the higher the number of clusters identified. While this would offer the possibility of identifying groups of participants in more detail, the clinical significance of a more detailed classification of neck pain based on the course of the disease is limited considering the current evidence on treatment alternatives. The reason for choosing such a model should be to facilitate visualization of the data. With that in mind, further analyses (identifying characteristics associated with courses of neck pain) were done using broad categories: favorable and unfavorable.

6.2.2. Post-randomization factors. Should they be considered?

In the protocol of the STONE trial⁸⁷ it was mentioned that an adjustment for expectations on the treatment would be performed. However, the results presented in Study II were not adjusted. The decision of adjusting or not for variables different from the treatment to which participants were randomized depends on the topic of exploration and what is understood as the *effect of the intervention*.

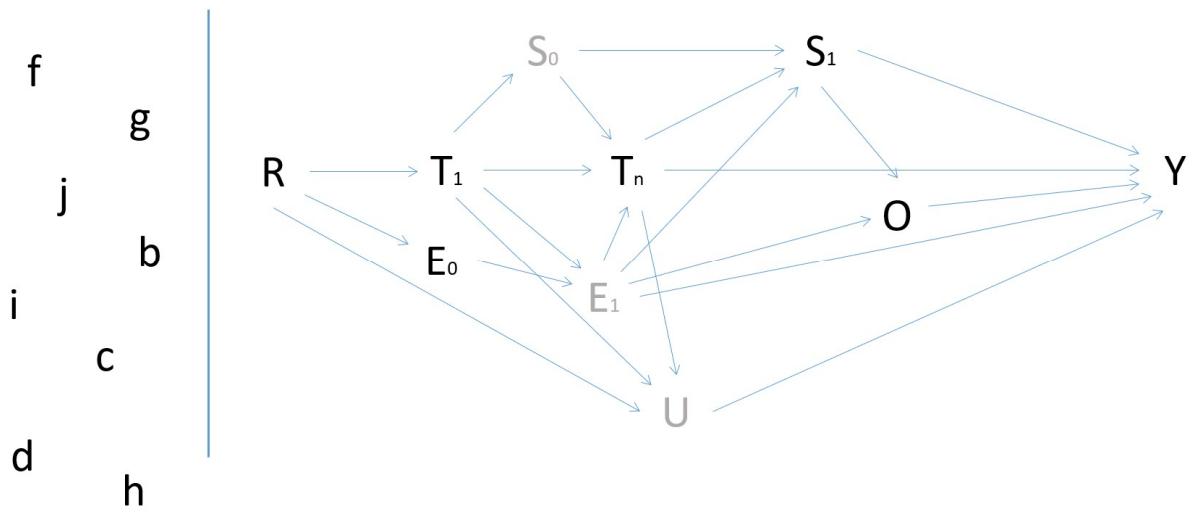
As mentioned in the methods section, we aimed to analyze the data following an intention to treat approach. However, there is another approach that is often not present in the literature called the per-protocol approach. This approach intends to control for imbalances in terms of potential confounding variables before or after the randomization. Unlike the intention to

treat approach, the per-protocol approach does not assume that: (1) all the participants in a trial adhered to the assigned treatment as indicated, (2) that they did not use any other concomitant treatment, or (3) that all groups were affected similarly by external factors such as satisfaction with the treatment or adverse events. Although it may be appealing to prefer a per-protocol approach to find out the “actual effect” of an intervention, it is difficult to control for all potential factors and, therefore, the intention to treat approach is often preferred and required.⁸⁸

When the STONE trial was designed, it was proposed to adjust for expectations. This was based on the reasoning that it would shed light on the direct effect of the interventions by taking away a psychological or behavioral component to either identify the biological/mechanical effect of the interventions and understand *how* the intervention works. However, apart from expectations, other factors that were measured during the follow-ups could (and must) have been considered to achieve that objective. These factors included: satisfaction with the treatment provided, adherence to the therapies and use of healthcare services (e.g. appointments with other healthcare providers).

For per-protocol analyses, two main groups of factors are commonly considered: pre-randomization factors and post-randomization factors. Pre-randomization factors are those measured at baseline. In STONE, it was assumed that the randomization would, by chance, distribute measured and unmeasured confounders to the four treatment equally and therefore no further adjustment for pre-randomization confounders would be necessary. Post-randomization factors, on the other hand, refer to factors that took place after participants were randomized to the different therapies, which would be necessary to adjust for in this case. A depiction of how those factors would interplay is presented in Figure 6.

Figure 6. Interplay of factors post-randomization in the STONE trial.



Lower case letters: Confounding factors before randomization. The line to the right aims to represent that pre-randomization confounding factors have no effect after that point. R: Randomization. T₁: First session of therapy as determined by the randomization. T_n: Consequent n number of therapies. E₀: Measured expectations on improving by effect of the assigned treatment. E₁: Unmeasured expectations of improving. S₀: Unmeasured satisfaction with the assigned therapy after the first session of therapy. S₁: Satisfaction with the therapies after completion. O: Other treatments received. U: Unmeasured confounding variables. Y: Outcomes to assess the effectiveness of the therapies.

In STONE, with no exception, the first session of therapy was actually given immediately after the randomization. It could be the case that after the first session, there was a change in the expectations on recovery due to treatment, which may have affected the adherence to the remaining sessions of therapy (for instance, not doing the recommended home exercises). In addition, satisfaction with the treatment also evolves over time. Although participants were advised not to use other forms of treatment during the first three months, they were free to do so if desired. In the ideal scenario, the sessions of therapy would be the only therapy that participants receive during the 52 weeks follow-up. However, some participants used additional treatments and visited other providers during that year.

Table 6 illustrates differences between groups in selected post-randomization variables. Expectations of being helped by the treatment (measured immediately after disclosing the

assigned treatment), were lower in the group assigned to advice to stay active, and similar among the other three groups. Likewise, satisfaction with the treatment, measured at seven weeks once all the sessions were provided, was lower in the advice group and comparable among the other three. Interestingly, in Study II, we found a positive effect of massage and combined therapy at seven weeks compared to advice (RR 1.36, 95% CI: 1.04-1.77 and RR 1.39, 95% CI: 1.08-1.81, respectively). It is likely that the reported higher level of satisfaction is the result of higher decrease in pain in those two groups. However, we cannot rule out that a feeling of satisfaction or wellness had led the participants to report lower levels of pain. Regardless of this, it is not necessary to unlink merely physiological effects from effects mediated through such feeling of wellness.

Furthermore, despite the recommendation of abstaining from visiting other healthcare providers during the first three months of the follow-up, we observed that those in the advice group did so to a greater extent and more often than the other three groups. It is, however, not possible to know the influence of such additional visits on the outcomes that were measured in the STONE trial. If the additional therapies had a positive effect, there could be an underestimation of the treatment effects. The opposite could also be true.

Table 6. Expectations on the treatment right after randomization, satisfaction with the treatment at seven weeks follow-up and use of other healthcare services at three months.

	Advice	Massage	Exercises	Combined therapy
Expectations on the treatment, median (p25-p75)*	5 (3-7)	7 (6-8)	7 (5-8)	8 (7-9)
Satisfaction with the treatment at seven weeks, median (p25-p75)†	5 (2-7)	8 (7-10)	7 (5-8)	8 (7-9)
Number of visits to other healthcare providers, at 3 months, mean (SD)‡	1.8 (3.6)	1.0 (3.0)	0.9 (2.4)	0.6 (1.9)
Proportion visiting another provider at least once, at three months‡	38%	26%	27%	19%

*Expectations on the treatment were measured with a numeric rating scale (NRS) from 0 to 10 immediately after revealing the assigned treatment. †Satisfaction was measured with a numeric rating scale from 0 to 10 at 7 weeks. ‡Other healthcare providers include: medical doctors, chiropractors, other naprapaths, physiotherapists, osteopaths, masseurs, personal trainers, and others.

Although the results at seven weeks are probably not unaffected by such interplay of factors, the ones at later follow-ups are likely more heavily influenced by post-randomization variables. Advanced methods such as g methods can control for those additional factors after the randomization and would show more “precise” results. However, such analyses are beyond the scope of this thesis. Furthermore, it depends on the research question whether adjustment should be made or not. In the STONE trial, the aim was to determine the effectiveness of the therapies regardless of whether the – possibly – observed effect was due to other factors than the biological or biomechanical effects of the interventions, in which case, not adjusting for post-randomization variables was more appropriate.

6.2.3. Potential sources of bias in randomized controlled trials

STONE was designed as a four-arm RCT. This design is deemed as the gold standard in medical research to assess the effect of interventions since it is characterized by a strive for maximum control of the way the intervention is provided and the surroundings. While it has developed quickly in the pharmaceutical field, it has been more challenging for non-pharmaceutical interventions to fulfill such rigourousness⁸⁹ given the complexity of the interventions.⁹⁰ For these reasons, it is necessary to consider limitations and sources of bias.^{89,91}

6.2.3.1. Trial selection bias

Selection bias occurs when the person in charge of enrolling study participants selects them based on the most likely coming treatment allocation and is characteristic of designs with a sequential treatment allocation.⁹² For instance, if the recruiter knows that fewer patients have been allocated to the active arms of the trial, they might recruit those in higher need of treatment, leading to biased results due to confounding derived from imbalances between the treatment arms. In STONE, various actions were taken to prevent this from happening. First, the randomization was done prior to the start of the recruitment. The pieces of paper indicating the treatment were folded twice and put in envelopes that were thereafter sealed. It would have been very difficult for the recruiter to guess which treatment belonged to each envelope. Second, the randomization was revealed when the participants visited the study clinic (when baseline questionnaire B was filled out), by the therapists, not by the study coordinator, who was completely unaware of the sequence. Since there were 30 different therapists, it was difficult for them to keep track of how previous participants had been allocated as the turnover of therapists was relatively high. Third, a checklist with well-defined inclusion criteria was applied to every potential participant. Finally, it was confirmed that there were no differences in terms of baseline pain intensity or pain-related disability between the arms.

6.2.3.2. Lack of blinding and unclear outcome definition

In blinded trials, participants and/or clinicians are not aware of which treatment is being received or given. In non-pharmacological interventions, it is often unfeasible to blind healthcare providers or participants (in the pharmacological field, this is known as open-label trial)⁹³, risking the validity of the study.

There are three levels of recommendations applicable to open-label trials to compensate for the lack of blinding: the first is to have a blinded external clinician/researcher assessing the outcome; if this is not possible, an external adjudication committee independent of the study can review each case and decide on the outcome.⁹⁵ A third alternative is to utilize an objective predefined set of criteria to minimize the subjectivity of the evaluation of the outcome as much as possible.⁹⁵

In the STONE trial, self-reported pain was the best approximation to the construct “pain” and, therefore, the first two strategies discussed above could not have been applied since it is unfeasible to assess or objectively confirm somebody’s pain experience. Instead, valid instruments were used to assess the primary outcomes. They were measured with a numeric rating scale (NRS) ranging from zero to ten, using an adapted version of the chronic pain grade questionnaire⁶⁸. The NRS is considered the best method for estimation of pain compared to the visual analogue scale and verbal rating scale.⁹⁶ In addition, a definition of successful perceived recovery as “completely recovered” or “much improved” has been used previously as a benchmark in connection to changes in the NRS for neck pain.⁹⁷ Cutoffs have been discussed in the literature to define successful cases of minimal clinically important improvement.

Using the receiver operating characteristic (ROC) curve, a study determined 2.5 as the cutoff point for NRS for pain intensity. At this point, false positives and false negatives were balanced and it was also considered relevant by patients.⁹⁷ Another study including patients seeking care for subacute or chronic pain found various minimal detectable change cutoffs based on the ROC curve method. These cutoffs varied from 1.5 to 2.5 depending on the baseline severity (the higher the baseline pain intensity, the higher the cutoff), and around 0.5 for patients with subacute pain and 1.5 chronic pain.⁹⁸ It should be noted that the cited studies included patients with pain intensity of at least 3/10 at enrolment. Another approach found in the literature on therapies for spinal pain is to define minimal clinically important change as a decrease of at least 30% of the baseline value.⁹⁹ The cutoffs of at least two points’ decrease in a NRS from 0 to 10 for pain intensity and at least one point for pain-related disability have also been proposed for spinal pain¹⁰⁰ and previously applied in the evaluation of non-pharmacological interventions.¹⁰¹ The latter was chosen to define the primary outcomes in the STONE trial.

An *a posteriori* calculation of the effect estimates of the therapies based on the outcome minimal clinically important improvement is presented in Table 7 to explore whether the

choice of another cut-off would have affected our conclusions. Whilst the effect sizes would have been smaller, differences from the original calculations are minimal and are in line with the conclusions of the STONE trial.

Table 7. Effect sizes for pain-intensity based on two units and 30% decrease from baseline to define minimal clinically important improvement.

	Massage		Exercise		Combined therapy	
	RR	95% CI	RR	95% CI	RR	95% CI
Minimal clinical important improvement of pain using 2-unit decrease cut-off						
7 weeks	1.36	1.04-1.77	1.14	0.86-1.51	1.39	1.08-1.81
12 weeks	1.09	0.85-1.39	1.00	0.78-1.29	1.28	1.02-1.60
26 weeks	1.23	0.97-1.56	1.31	1.04-1.65	1.15	0.90-1.46
52 weeks	1.03	0.83-1.29	1.11	0.90-1.37	1.10	0.89-1.35
Minimal clinical important improvement of pain using 30% decrease cut-off						
7 weeks	1.32	1.03-1.69	1.15	0.88-1.49	1.34	1.06-1.72
12 weeks	1.07	0.88-1.29	0.98	0.80-1.19	1.12	0.94-1.35
26 weeks	1.07	0.88-1.30	1.17	0.97-1.41	1.09	0.91-1.32
52 weeks	0.99	0.81-1.20	1.05	0.87-1.26	1.03	0.85-1.26

Additionally, in the cost-effectiveness analysis, the EQ-5D questionnaire was used.⁷⁰ EQ-5D is a valid instrument for populations with chronic pain and sensitive to changes in the condition.¹⁰² Although some efforts have been made to find a minimal clinically important change for EQ-5D values, such values are not widely accepted, and therefore, it was not considered in the economic evaluation.¹⁰³

6.2.3.3. Choice of comparison group

There is no gold standard in rehabilitative therapies.¹⁰⁴ The choice of the control group should depend on the research question(s), the intervention(s) being evaluated and on the factors one wishes to control for.⁹³ Such a choice will affect the interpretation of the results. In the STONE trial, a widely accepted intervention was chosen.³⁰ Other existing alternatives were the inclusion of more than one control group such as usual care and pure placebo; or to add the placebo component to all arms, including the comparison group.⁹³ The inclusion of more

than one control would have been difficult in STONE considering the costs of recruiting 150 additional study participants and the potential risk of attrition, given the long follow-up time.

The two main challenges we observed in STONE are: first, it is impossible to infer how good the interventions were compared to leaving the participants completely untreated, and, second, the effectiveness of the comparison group “advice to stay active” has been debated^{36,37}. This is, however, due to a – justified – lack of uniformity in the way advice therapy is given. For example, advice can refer to written instructions, a video, a conversation with a professional in the emergency room or more comprehensive sessions such as the ones provided in the STONE trial, which we hypothesize are better than what is actually seen in the usual clinical practice. Therefore, when interpreting the main results of the present trial, it is necessary to bear in mind that they are always in comparison to the reference intervention provided.

Unfortunately, for the between-group comparison of adverse events, there was no specific control group defined, and therefore we performed multiple comparisons. Furthermore, although it would have been very informative to measure adverse events in the advice group, we anticipated lack of response and therefore they were excluded from this aspect of the evaluation.

6.2.3.3.1. Placebo control

In pharmacologic trials, a good placebo is one that looks, smells and tastes the same as the experimental treatment, while having no active ingredients, and should be given in the same setting as the experimental group. A placebo for non-pharmacological interventions is more complex since factors beyond the sensory ones should be considered. These factors include performance bias and expectations for success from both the practitioner and the patient.⁹³ In a systematic review comparing placebo versus no treatment, placebo had a better effect for continuous outcomes, especially for subjective ones such as pain.¹⁰⁵ In a hypothetical scenario in which a placebo for deep tissue massage and exercise was to be created, exact knowledge on the active ingredients mediating the effect of these therapies would be needed. This is, however, far from becoming a reality anytime soon.

A placebo has various components such as expectations from the patient and the provider, and the result of the interaction between patient and their environment.⁹³ A way of counteracting the willingness of the patient to please the provider is by highlighting that the effect of the therapy is unknown. When novel interventions are tested, apprehensions among

those ending up in that arm can occur. On the other hand, well-accepted interventions or those which participants are likely to know in advance, may generate high expectations. Such an introduction of elements (such as expectations) post randomization is known as *performance bias*. These elements may originate both from the therapist and the participant.¹⁰⁶ In the STONE trial, adjusting for factors such as expectations and satisfaction could have, at least partially, accounted for the placebo's components. However, as discussed in previous sections, the need for disentangling merely biological or mechanical factors from factors that belong to the spectrum of placebo, is debatable.

A strategy to deal with placebo effects is to identify study participants who are likely to show high responses to placebo interventions and exclude them from the trial. Such identification can be done by giving a placebo treatment during the run-in period immediately before the official start of the trial. However, this is challenging to apply in practice.⁹³ Another strategy is to use a wait-list control. Nonetheless, applying these strategies would have been very costly, time consuming and would result in higher attrition rates.

6.2.3.4. Poor standardization of the interventions

The delivery of the interventions should be as standardized as possible.⁹³ The purpose of this is to ensure that any eventual positive or negative effect can be attributed to a well-defined intervention or active ingredient. In the STONE trial, various levels of exercise and/or intensity of the massage were employed, instead of a single standardized one. However, eventual variations were also guided by the protocol. Additional information on the muscles targeted and on the level of intensity – for the exercise and combined therapy groups – was collected from the medical records for each patient. It is possible that positive effects are only observed, for instance, at certain levels of exertion. However, investigating this is outside the scope of this thesis. Even though various sessions of training prior to trial start and during the inclusion period were given to the therapists, complete standardization was probably not achieved given the complex nature of the condition and the virtually infinite possibilities of interactions between patient and therapist.

6.2.3.5. Attrition bias

Differential attrition may or may not result in biased estimates.¹⁰⁷ Attrition bias occurs if the dropouts are determined by the outcome; that is to say, those with poorer outcomes are more likely to dropout, regardless of which arm they belong to. However, the risk of bias could be

minimized if the attrition is similar across all groups. Reasons for the dropouts should be given and the analyses should follow an intention to treat approach.¹⁰⁸

While no differences in terms of baseline variables were observed between dropouts and those who remained in the STONE trial, it is possible that they differed in characteristics not measured in the questionnaires, such as catastrophizing or self-efficacy. Those in the advice to stay active group were more likely to drop out than in the other groups, probably because the intervention was not considered novel. If those leaving the control arm had worse outcomes (in which case, it would be *missing not at random*), the estimated effect of the experimental arms would be underestimated. The opposite could also be true. Methods to control for such missing data include single imputation and multiple imputation. These methods were not used in the sub-study of effectiveness of the therapies. However, multiple imputation was used in the health economic evaluation, in which costs and outcomes were imputed under a theoretical assumption that the data was missing at random.

6.2.4. Generalizability of the findings from the STONE trial

There is, in theory, a distinction between pragmatic and efficacy or explanatory trials, but in practice, most trials lie on a continuum between the two. On the ‘efficacy’ end, we have studies that aim to determine how an intervention works regarding biological mechanisms. On the ‘pragmatic’ end, we have trials whose aim is to show how that intervention can be applied in daily practice by investigating the effectiveness, safety and cost-effectiveness of the interventions.

Various features determine whether a study is designed more as a pragmatic or an efficacy trial (Table 8). The interventions evaluated in the STONE trial are complex because they involve interactions between the therapist and the participants. In addition, neck pain is a multifaceted condition for which its mechanisms have not been fully elucidated yet and there is no gold standard for treatment. For these reasons, the STONE trial was largely designed with mostly pragmatic features. This is very valuable from a practical perspective, since results are more generalizable and easier to implement. The following table presents an assessment of the level of pragmatism for nine criteria. The possible assessments are: very pragmatic, rather pragmatic, equally pragmatic/explanatory, rather explanatory and very explanatory.¹⁰⁹

Table 8. Aspects to assess the pragmatism of trials based on the PRECIS-2 tool¹⁰⁹.

Dimension	Assessment of pragmatism	How it looked in the STONE trial
Recruitment of investigators and participants		
Eligibility	To what extent are the participants in the trial similar to patients who would receive this intervention if it was part of usual care?	<p>General inclusion/exclusion criteria were applied (for instance, wide age range, whiplash associated or not, with neurologic symptoms or not). On the other hand, a third of those who contacted the study coordinator were not willing to complete the procedures of the trial. It is likely that those finally included in the trial were a selected group (e.g. more health conscious or compliant).</p> <p>Level of pragmatism: Rather pragmatic</p>
Recruitment	How much extra effort is made to recruit participants over and above what would be used in the usual care setting to engage with patients?	<p>The STONE trial had to be announced in newspapers and to reach the calculated sample size, two public companies were contacted.</p> <p>Level of pragmatism: Rather explanatory</p>
Setting	How different are the settings of the trial from the usual care setting?	<p>The usual providers of therapies in this trial were very heterogeneous. Multiple providers such as physiotherapists, chiropractors, masseurs or personal trainers can provide at least one of the therapies in the STONE trial. In the STONE trial, there were only naprapaths with a similar training.</p> <p>Despite this, there was a high degree of variability since there were 30 different therapists involved, and heterogeneity in the provision of the therapy based on the patient's characteristics was encouraged and expected to have occurred.</p> <p>Level of pragmatism: Equally pragmatic/explanatory</p>

The intervention and its delivery within the trial

Organization	How different are the resources, provider expertise, and organization of care delivery in the intervention group of the trial from those available in usual care?	<p>Therapists had variable degrees of expertise reflecting the usual practice. The delivery of the interventions was done as usual at the clinic.</p> <p>Level of pragmatism: Rather pragmatic</p> <p>Unlike the procedures in the STONE trial, systematic recording of adverse events or quality of life is not part of the usual clinical practice, but it is very often considered.</p> <p>Level of pragmatism: Equally pragmatic/explanatory</p>
--------------	-------------------------------------------------------------------------------------------------------------------------------------------------------------------	--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------

Flexibility in the delivery	How different is the flexibility in how the intervention is delivered from the flexibility anticipated in usual care?	<p>It was flexible. Therapists adapted the intensity of the massage and exercises according to the tolerance and ability to perform, respectively. Similarly, those in the advice group received more focus on what they needed the most. Participants were advised to abstain from other therapies, but were free to do so if desired.</p> <p>Level of pragmatism: Rather pragmatic</p>
-----------------------------	-----------------------------------------------------------------------------------------------------------------------	-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------

Flexibility in adherence	How different is the flexibility in how participants are monitored and encouraged to adhere to the intervention from the flexibility anticipated in usual care?	<p>Participants were encouraged to attend all the programmed sessions from the beginning of the trial.</p> <p>Level of pragmatism: Rather pragmatic</p>
--------------------------	-----------------------------------------------------------------------------------------------------------------------------------------------------------------	----------------------------------------------------------------------------------------------------------------------------------------------------------------

The nature of follow-up

Follow-up	How different is the intensity of measurement and the follow-up of participants in the trial from the typical follow-up in usual care?	<p>We had regular measurements, in addition to the questionnaires at the pre-specified time points, there were text messages sent every week for one year. In addition, we had questionnaires about adverse events during the delivery of the therapies and the follow-up. There was a person in charge of reminding the participants to answer to the questionnaires and text messages.</p> <p>Level of pragmatism: Rather explanatory</p>
-----------	----------------------------------------------------------------------------------------------------------------------------------------	----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------

The nature, determination, and analysis of outcomes

Primary outcome	To what extent is the primary outcome of the trial directly relevant to participants?	The primary outcomes in Study I were minimal clinically important improvement in pain intensity and minimal clinically important improvement in pain-related disability, which were very important for participants. Level of pragmatism: Very pragmatic
-----------------	---------------------------------------------------------------------------------------	------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------

Primary analysis	To what extent are all data included in the analysis of the primary outcome?	Attrition was low. We followed an intention to treat approach. Level of pragmatism: Rather pragmatic
------------------	------------------------------------------------------------------------------	--------------------------------------------------------------------------------------------------------------------

As can be concluded from the table above, despite being a predominantly pragmatic trial, various adjustments appropriate to an explanatory trial had to be implemented to ensure high quality and good internal validity of the study. Despite this, the findings from the STONE trial are highly generalizable to the target population.

The participants of STONE were recruited from the general population, instead of a care-seeking population. A proportion of participants would have never sought care for neck pain or might have done so at later stages of the condition, if persisting. This means that cases included in the STONE trial may have been milder than what is usually seen in clinical practice. Furthermore, the study population was probably more self-aware since they were willing to be monitored intensively for one year, and therefore, more compliant.

The therapies were provided at one single center and all the therapists were naprapaths. Although there were variations in the way the therapies were provided, it is possible that further variations would occur if other professionals provided (as it is the case in practice) the same interventions.

Intensive measurement was necessary to collect data for the description of the course of the condition and for the assessment of the outcomes at different time points. Although such regularity of measurements is not the usual practice, it is well justified since it is the only way of monitoring the response over time.

6.2.5. Additional considerations

6.2.5.1. Priming and information bias in the reporting of harms

Participants in the trial could have never reported adverse events (AE) unless given the opportunity to do so with a questionnaire (effect known as *priming*).¹¹⁰ Therefore, we cannot rule out the risk of overestimation of the incidence of AE. Some AE reported by participants in our trial are common symptoms of neck pain. For example, a headache is a condition that is often associated with neck pain.¹¹¹ The question is whether the provision of the therapies actually resulted in the debut of headache as an adverse event or if it was in fact an exacerbation of a pre-existing condition. A possible solution would be to identify (and possibly exclude) those participants more likely to build expectations around the effect of an intervention (as mentioned in section 6.2.4.3.1. *Placebo*), but this would require a larger investment of resources. Furthermore, given the scarcity of literature on the topic, it is hard to contrast the observed incidence of AE with the previous reports.

It is also possible that some participants did not recall information on debut, duration and/or degree of AE with precision. This, however, would have resulted in a non-differential misclassification.

6.2.5.2. Comparison of benefits and harms

It can be debated whether benefits and harms should be combined together considering that these components might not be placed in the same scale.¹¹² In the STONE trial, participants were actively asked about the different types of adverse effects and that information was used to construct the measures of association: number needed to treat, number needed to harm and likelihood to be harmed versus helped.^{113,114} Such measures are reported in a concrete intuitive way and are often presented in clinical trials.¹¹³ However, they can vary depending on the magnitude of the baseline risk, do not specify if those who are harmed are also those who benefit, and might be subject to, the specific context in which the data were collected, for example in an experimental setting such as in a RCT.¹¹³

6.2.5.3. Considerations for the health economic evaluation of the STONE trial

Data on costs and use of health services were collected during the conduction of the STONE trial. Health economic evaluations alongside trials offer the benefit of collecting data at a reduced cost compared to a study with the only aim of conducting an economic evaluation

and following the rigorous protocol of an RCT. On the other hand, various challenges exist.¹¹⁵

One of the most commonly discussed challenges is that, in RCTs, care is protocol-driven and does not reflect the routines in clinical practice, which are often less intensive, thus limiting the generalizability of economic outcomes. Patient compliance is actively encouraged and therefore higher than in real settings where patients do not receive an equal level of guidance. This might result in either increased estimation of costs, as a result of the enforced compliance, or underestimation of long-term costs of complications associated with better outcomes occurring in controlled settings. An additional risk of bias is due to an excessive active case finding, which would not have come to the attention of the clinicians otherwise. Furthermore, in RCTs, all treatment arms go through similar procedures or tests to ensure uniformity, but this is also not the case in clinical practice.¹¹⁵ As discussed above, the STONE trial has many pragmatic elements in its design, which make the results more generalizable.

Likewise, the chosen time horizon in economic evaluations carried along RCTs might be a source of error. Clinical trials are sometimes stopped before clinically important differences are detected, especially in RCTs for chronic conditions.¹¹⁵ Whilst neck pain is often a persistent condition, a period of one year was considered appropriate to capture relevant information.

6.3. Summary of findings

Finally, based on the findings of the STONE trial, what would the recommendation be for different stakeholders? A summary of the main findings is presented in Table 9.

Table 9. Summary of findings of the STONE trial.

	Advice to stay active	Deep tissue massage	Strengthening and stretching exercises	Combination of exercises and massage
Primary outcomes	Used as the reference group	Similar reduction in pain intensity at one year as advice but better in the short term No differences in pain-related disability	Similar reduction in pain intensity at one year as advice but better in the mid-term No differences in pain-related disability	Similar reduction in pain intensity at one year as advice but better in the short term No differences in pain-related disability
Secondary outcomes	Used as the reference group	Better self-perceived recovery than advice at all follow-ups Higher sickness-absence than the advice group	Better self-perceived recovery than advice at all follow-ups Higher sickness-absence than the advice group	Better self-perceived recovery than advice at all follow-ups Higher sickness-absence than the advice group
Harms	Unknown	Probably more adverse events than exercise	Used as the reference group	Probably similar to exercise
Costs and gains in quality of life	Inexpensive	More costly and less gains in quality-adjusted life years than advice	Probably cost-effective compared to advice	More costly and less gains in quality-adjusted life years than advice

6.3.1. Messages for persons with non-specific neck pain

- Massage may help to slightly decrease your pain shortly after completing the sessions. Neck exercises may help to slightly decrease your pain a few months after completing the sessions. Combining the two therapies could provide similar pain reduction in pain of massage alone or exercise alone.

- Despite not seeing large improvements in pain, using massage and/or neck exercises will make you feel improved, especially during the first weeks after receiving therapy.
- Those interventions might cause you some discomfort and unwanted adverse effects such as tiredness, muscle soreness, increased pain, but are generally safe.
- It is also possible that pain may not go away or improve very little, despite receiving any of the mentioned therapies.
- Exercise and advice are inexpensive alternatives. Massage and a combined therapy are more costly.

6.3.2. Messages for health professionals and decision-makers

- Patients should be informed of the possibility that no improvement in pain intensity and pain-related disability may result despite receiving these treatment modalities.
- If deep tissue massage is provided, a decrease of pain-intensity in the short term may result, but patients should be informed of the lack of effects in the long term. However, perceived recovery is likely to occur in the short term and even in the long term.
- If strengthening and stretching exercises are given as treatment, a decrease of pain-intensity in the mid-term may result. Patients should be informed of the lack of effects in the long term. However, a feeling of perceived recovery is likely to occur starting in the short term and even in the long term.
- If deep tissue massage combined with strengthening and stretching exercises are given as treatment, a decrease of pain-intensity in the short and mid-term may result, but patients should be informed about the lack of effects in the long term. However, perceived recovery is likely to occur starting from the short term and even in the long term.
- Advice alone is discouraged when there is access to any of the other treatment alternatives mentioned here.
- Information on adverse events should be considered when choosing between these therapies. Patients can be reassured that the therapies are safe, but that they will be likely to experience non-serious adverse events.
- Strengthening and stretching exercises are cost-effective at one year from a societal perspective compared to advice. Deep tissue massage and a combination of both modalities are more expensive and are not associated with more gains in quality of life than advice.

7 ETHICAL CONSIDERATIONS

Equipoise in RCTs is defined as the researcher's genuine belief that treatments are comparable. That includes situations when there is uncertainty due to a lack of previous evidence even when the researcher suspects there might be differences.¹⁰⁴ In STONE, previous knowledge from the Björn trial¹⁰¹ showed that naprapathic manual therapies were better than advice but, in that case, no individual components were examined and there was no certainty around which individual therapies would work.

In ethics, a violation occurs when there is lack of respect for a patient's autonomy and it can be either subjective or objective.¹¹⁶ Considering that the measures in STONE were collected repeatedly over the course of a year, two aspects are worth mentioning. The first concerns the potential violation of participants' privacy and the second concerns potential harms associated with the intensive data collection method. Despite the fact that the subjects gave their consent and received relevant information about the study, the frequency and length of the data collection might have seemed intrusive. Participants might have experienced a sense of being "in debt" and felt the need to please or pay back by responding to the questionnaires and messages during follow-up. They might have also felt psychologically exhausted due to the large number of times they received an SMS with the same questions every week for a year. Factors that likely contribute to exhaustion include: the length and frequency of the questionnaires, the participant's general status, and the type of questions.¹¹⁷ In the STONE trial, the questionnaires were not extensive, and the text messages contained two short questions, for which the answer was a number between 0 and 10, which can be considered simple and expedited.

The SMS may have acted as a reminder of pain, meaning that we could have potentially caused even more harm to participants instead of just evaluating the normal course of the disease. Asking about this could somehow intensify pain experiences, and, in that case, participation in the study would have been harmful. The individual subjective appreciation of symptoms has been explored on patients with cancer and other chronic diseases in the setting of data collection.¹¹⁸ Interviews, for instance, usually contain personal aspects in a much deeper way than questionnaires but at the same time offer an opportunity to provide support or create a good relationship between interviewers and participants.¹¹⁹ Studies exploring whether using frequent measurements of pain and fatigue triggered negative feelings in

patients with musculoskeletal disorders found that it was not the case and that, in fact, these frequent measurements could actually reduce the reporting of depressive symptoms.¹²⁰

The STONE trial complied to current guidelines regarding storage of data and management of personal information. Paper questionnaires were scanned and stored in a secure server at the Institute of Environmental Medicine, at Karolinska Institutet.

8 CONCLUSIONS

- Neither deep tissue massage, nor supervised strengthening and stretching exercises, or a combination of both, were better than advice at achieving minimal clinically important improvements in pain intensity or pain-related disability at one year.
- A proportion of participants did not benefit or benefited less from the therapies provided. Women, those with higher pain intensity and depressive symptoms at enrollment, younger persons and those with sudden onset of pain were more likely to report unfavorable pain trajectories.
- Effects in terms of minimal clinically important improvement in pain intensity were seen in the short or mid-term, and self-perceived recovery was better in the index therapies than in the reference group advice to stay active, in the short and long term.
- Adverse events were common but not serious. There were no differences in the benefit/harm profile between the therapies evaluated in this trial.
- Supervised strengthening and stretching exercise therapy was found to be cost-effective compared to advice to stay active, if the willingness to pay by society is above 175,295 Swedish crowns (17,640 EUR). Deep tissue massage alone or combined with exercises were more costly and associated with slightly less gains in quality of life than advice.

9 FUTURE PERSPECTIVES

Different modalities of massage and exercise are commonly used to treat neck pain^{121,122}. Patients with neck pain often take different routes to come into contact with professionals providing such therapies. Data have shown that few patients are directly referred to manual therapists.^{123,124} With this in mind, active participation of patients and different actors in the healthcare sectors should be encouraged, ideally from early stages of the research process.¹²⁵

The use of advice to stay active only as reference group should be reconsidered in future trials. Instead, non-inferiority or superiority trials could use active treatments (such as the index therapies of the STONE trial) as comparators. Such practice can offer more valid results and increase the body of evidence. In addition, for future studies, a good balance of pragmatism and rigorousness should be part of the discussion at the planning stage. A well-designed cost calculation should also be planned at early stages of the trial.

Adverse events should be collected systematically alongside studies. In addition, active surveillance of adverse events should become a common practice in the field of musculoskeletal medicine.

10 ACKNOWLEDGEMENTS

I would like to thank the Swedish Research Council (VR), the Swedish Research Council for Health, Working Life and Welfare (FORTE) and the Swedish Naprapathic Association for funding the STONE trial.

Thanks to Eva Skillgate, Lena Holm, and Irene Jensen for their supervision, patience, guidance and motivation during the period in which I took part of this project as a doctoral student. Special thanks to Pierre Côté for being an unofficial supervisor and contributing with enriching feedback in all the papers included in this thesis.

Thanks to Anna Peterson for her invaluable work during the data collection of the STONE trial. To Peter Viklund, Martin Asker and Fredrik Johanson for their involvement in the planning stage of the logistic aspects of the STONE trial. Also, thanks to the naprapaths involved in the project.

Special thanks to the participants in the STONE trial. I hope this thesis contributes to increasing the knowledge on their condition and that they will eventually benefit from better care.

Thanks to all the co-authors of the papers for their input and contributions to improving the quality of every section of the manuscripts. Also, thanks to the editors and anonymous reviewers of the manuscripts included in this thesis.

Thanks to Tim Hustad from Totalkropp clinic and Lisa Apelgren from Danderyd Hospital for letting me observe their work with patients with neck pain.

Thanks to the members of the Musculoskeletal and Sports Injury Epidemiology Center for the discussions and feedback.

I would also like to thank Myriam Ruiz Rodriguez and Herman Jose Arteaga for inspiring me and encouraging me to develop my research skills. Special thanks to Sari Ponzer for helping me plan the next steps in my career.

Thanks to my dear friends and colleagues Alicia Nevriana, Marios Rosidess, Ying Shang, Andrea Cediél, Christiane Rudolph, German Carrasquilla, Åsa Persson, Vladimir Pabon and Kristoffer Bonde Poll for their constant support and for lifting me up. Thanks to other colleagues and friends I have met during my time at Karolinska Institutet for all the discussions and chats.

Finally, infinite thanks to my husband, my mother, my father, my sister and my extended family for encouraging me to be better every day.

11 REFERENCES

1. Wiitavaara B, Bengs C, Brulin C. Well, Im healthy, but. - Lay perspectives on health among people with musculoskeletal disorders. *Disabil Rehabil.* 2016;38(1):71-80. doi:10.3109/09638288.2015.1024338
2. International Association for the Study of Pain. Pain. IASP taxonomy. <http://www.iasp-pain.org/Taxonomy#Pain>. Published 2017.
3. Dinakar P, Stillman AM. Pathogenesis of Pain. *Semin Pediatr Neurol.* 2016;23(3):201-208. doi:10.1016/j.spen.2016.10.003
4. International Association for the Study of Pain. *Spinal and Radicular Pain Syndromes*; 2012.
5. Fejer R, Kyvik KO, Hartvigsen J. The prevalence of neck pain in the world population: A systematic critical review of the literature. *Eur Spine J.* 2006;15(6):834-848. doi:10.1007/s00586-004-0864-4
6. Hoy D, March L, Woolf A, et al. The global burden of neck pain: estimates from the global burden of disease 2010 study. *Ann Rheum Dis.* 2014;73(7):1309-1315. doi:10.1136/annrheumdis-2013-204431
7. Cohen SP. Epidemiology, Diagnosis, and Treatment of Neck Pain. *Mayo Clin Proc.* 2015;90(2):284-299. doi:10.1016/j.mayocp.2014.09.008
8. Skillgate E, Magnusson C, Lundberg M, Hallqvist J. The age- and sex-specific occurrence of bothersome neck pain in the general population--results from the Stockholm public health cohort. *BMC Musculoskelet Disord.* 2012;13:185. doi:10.1186/1471-2474-13-185
9. Vos T, Allen C, Arora M, et al. Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990-2015: a systematic analysis for the Global Burden of Disease Study 2015. *Lancet.* 2016;388:1545-1602. doi:10.1016/S0140-6736(16)31678-6
10. SBU. Ont i ryggen, ont i nacken. Sammanfattning och slutsatser En systematisk litteraturoversikt. *SBU.* 2000;(145/1).
11. Shahidi B, Curran-everett D, Maluf KS. Psychosocial, Physical, and Neurophysiological Risk Factors for Chronic Neck Pain: A Prospective Inception Cohort Study. *J Pain.* 2015;16(12):1288-1299. doi:10.1016/j.jpain.2015.09.002
12. Manchikanti L, Singh V, Datta S, Cohen SP, Hirsch JA. Comprehensive review of epidemiology, scope, and impact of spinal pain; *Pain Physician.* 2009;12:E35-E70.
13. Paksaichol A, Janwantanakul P, Purepong N, Pensri P, Beek A van der. Office workers' risk factors for the development of non-specific neck pain: a systematic review of prospective cohort. *Occup Env Med.* 2012;69:610-618.
14. Bohman T, Côté P, Boyle E, Cassidy JD, Carroll LJ, Skillgate E. Prognosis of patients with whiplash-associated disorders consulting physiotherapy: Development of a predictive model for recovery. *BMC Musculoskelet Disord.* 2012;13. doi:10.1186/1471-2474-13-264

15. Feleus A, Bierma-Zeinstra SMA, Miedema HS, et al. Prognostic indicators for non-recovery of non-traumatic complaints at arm, neck and shoulder in general practice - 6 months follow-up. *Rheumatology*. 2007;46(1):169-176. doi:10.1093/rheumatology/kel164
16. Karels CH, Bierma-Zeinstra SMA, Burdorf A, Verhagen AP, Nauta AP, Koes BW. Social and psychological factors influenced the course of arm, neck and shoulder complaints. *J Clin Epidemiol*. 2007;60(8):839-848. doi:10.1016/j.jclinepi.2006.11.012
17. Rasmussen-Barr E, Grooten WJ a, Hallqvist J, Holm LW, Skillgate E. Are job strain and sleep disturbances prognostic factors for neck/shoulder/arm pain? A cohort study of a general population of working age in Sweden. *BMJ Open*. 2014;4(7):e005103. doi:10.1136/bmjopen-2014-005103
18. Bohman T, Alfredsson L, Jensen I, Hallqvist J, Vingård E, Skillgate E. Does a healthy lifestyle behaviour influence the prognosis of low back pain among men and women in a general population? A population-based cohort study. *BMJ Open*. 2014;4(12):e005713. doi:10.1136/bmjopen-2014-005713
19. Guzman J, Haldeman S, Carroll LJ, et al. Clinical Practice Implications of the Bone and Joint Decade 2000 –2010 Task Force on Neck Pain and Its Associated Disorders From Concepts and Findings to Recommendations. *Spine (Phila Pa 1976)*. 2008;33(45):S199-S213.
20. Chevan J, Riddle DL. Factors Associated With Care Seeking From Physicians, Physical Therapists, or Chiropractors by Persons With Spinal Pain: A Population-Based Study. *J Orthop Sport Phys Ther*. 2011;41(7):467-476. doi:10.2519/jospt.2011.3637
21. Muller AE, Clausen T, Odsbu I, Skurtveit S. Observational study Prescribed opioid analgesic use developments in three Nordic countries , 2006 – 2017. *Scand J Pain*. 2019;19(2):345-353.
22. Dubin RE, Flannery J, Taenzer P, Smith A. ECHO Ontario Chronic Pain & Opioid Stewardship : Providing access and building capacity for primary care providers in underserved , rural , and remote communities. 2015. doi:10.3233/978-1-61499-505-0-15
23. Evidence based medicine working group. Evidence-Based Medicine. *JAMA*. 1992;268(16):2420-2425.
24. Heneghan C, Mahtani KR, Goldacre B, Godlee F, Macdonald H, Jarvies D. Evidence based medicine manifesto for better healthcare: A response to systematic bias, wastage, error and fraud in research underpinning patient care. *Evid Based Med*. 2017;22(4):120-122. doi:10.1136/ebmed-2017-j2973rep
25. Petticrew M. When are complex interventions “complex”? When are simple interventions “simple”? *Eur J Public Health*. 2011;21(4):397-398. doi:10.1093/eurpub/ckr084
26. Schünemann HJ. Methodological idiosyncracies, frameworks and challenges of non-pharmaceutical and non-technical treatment interventions. *Z Evid Fortbild Qual Gesundhwes*. 2013;107(3):214-220. doi:10.1016/j.zefq.2013.05.002
27. Wilson PR. Chronic neck pain and cervicogenic headache. *Clin J Pain*. 1991;7:5-11.

28. Barry M, Jenner JR. Pain in neck, shoulder, and arm. *BMJ*. 1995;310(January):183-186.
29. Sutton DA, Cote P, Wong JJ, et al. Is multimodal care effective for the management of patients with whiplash-associated disorders or neck pain and associated disorders? A systematic review by the Ontario Protocol for Traffic Injury Management (OPTIMa) Collaboration. *Spine J*. 2016;16(12):1541-1565. doi:10.1016/j.spinee.2014.06.019
30. Côté P, Wong JJ, Sutton D, et al. Management of neck pain and associated disorders: A clinical practice guideline from the Ontario Protocol for Traffic Injury Management (OPTIMa) Collaboration. *Eur Spine J*. 2016;25(7):2000-2022. doi:10.1007/s00586-016-4467-7
31. Hansson T, von Sydow H. Back and Neck Pain. In: *Läkemedelsboken*. Gothenburg, Sweden; 2015. https://lakemedelsboken.se/kapitel/rorelseapparaten/rygg-_och_nackbesvar.html?search=nack&id=p3_60#p3_60.
32. Southerst D, Nordin MC, Côté P, et al. Is exercise effective for the management of neck pain and associated disorders or whiplash-associated disorders? A systematic review by the Ontario Protocol for Traffic Injury Management (OPTIMa) Collaboration. *Spine J*. 2014. doi:10.1016/j.spinee.2014.02.014
33. Wong JJ, Shearer HM, Mior S, et al. *Are Manual Therapies, Passive Physical Modalities, or Acupuncture Effective for the Management of Patients with Whiplash-Associated Disorders or Neck Pain and Associated Disorders? An Update of the Bone and Joint Decade Task Force on Neck Pain and Its Ass.* Vol 16. Elsevier Inc.; 2016. doi:10.1016/j.spinee.2015.08.024
34. Patel K, Gross A, Graham N, et al. Massage for mechanical neck disorders. *Cochrane Database Syst Rev*. 2013;(9). doi:10.1002/14651858.CD001929.pub3.www.cochranelibrary.com
35. Gross A, Tm K, Jp P, et al. Exercises for mechanical neck disorders (Review) Exercises for mechanical neck disorders. *Cochrane Database Syst Rev*. 2015;(1):N.PAG-N.PAG. doi:10.1002/14651858.CD004250.pub5.Copyright
36. Gross A, Forget M, K SG, et al. Patient education for neck pain (Review). *Cochrane Database Syst Rev*. 2012;(3). doi:10.1002/14651858.CD005106.pub4.www.cochranelibrary.com
37. Yu H, Pierre C, Southerst D, et al. Does structured patient education improve the recovery and clinical outcomes of patients with neck pain ? A systematic review from the Ontario Protocol for Traffic Injury Management (OPTIMa) Collaboration ot. *Spine J*. 2016;16:1524-1540. doi:10.1016/j.spinee.2014.03.039
38. Driessen MT, Lin C-WC, van Tulder MW. Cost-effectiveness of conservative treatments for neck pain: a systematic review on economic evaluations. *Eur Spine J*. 2012;21(8):1441-1450. doi:10.1007/s00586-012-2272-5
39. Pach D, Piper M, Lotz F, et al. Effectiveness and Cost-Effectiveness of Tuina for Chronic Neck Pain: A Randomized Controlled Trial Comparing Tuina with a No-Intervention Waiting List. *J Altern Complement Med*. 2018;24(3):231-237. doi:10.1089/acm.2017.0209 LK
40. Hollinghurst S, Sharp D, Ballard K, et al. Randomised controlled trial of Alexander technique lessons, exercise, and massage (ATEAM) for chronic and recurrent back

pain: economic evaluation. *BMJ*. 2008;337:a2656.

41. Miyamoto GC, Lin C-WC, Cabral CMN, van Dongen JM, van Tulder MW. Cost-effectiveness of exercise therapy in the treatment of non-specific neck pain and low back pain: a systematic review with meta-analysis. *Br J Sports Med*. April 2018. doi:10.1136/bjsports-2017-098765
42. Korthals-de Bos IBC, Hoving JL, van Tulder MW, et al. Cost effectiveness of physiotherapy, manual therapy, and general practitioner care for neck pain: economic evaluation alongside a randomised controlled trial. *Prim Care*. 2003;326(April):1-6.
43. Landen Ludvigsson M, Peolsson A, Peterson G, Dederling A, Johansson G, Bernfort L. Cost-effectiveness of neck-specific exercise with or without a behavioral approach versus physical activity prescription in the treatment of chronic whiplash-associated disorders: Analyses of a randomized clinical trial. *Medicine (Baltimore)*. 2017;96(25):e7274. doi:10.1097/MD.00000000000007274
44. Velde G Van Der, Yu H, Paulden M, et al. Which interventions are cost-effective for the management of whiplash-associated and neck pain-associated disorders ? A systematic review of the health economic literature by the Ontario Protocol for Traffic Injury Management (OPTIMa) Collaboration. *Spine J*. 2016;16(12):1582-1597. doi:10.1016/j.spinee.2015.08.025
45. Maiers M, Bronfort G, Evans R, et al. Spinal manipulative therapy and exercise for seniors with chronic neck pain. *Spine J*. 2014;14(9):1879-1889. doi:10.1016/j.spinee.2013.10.035
46. Evans R, Bronfort G, Schulz C, et al. Supervised Exercise With and Without Spinal Manipulation Performs Similarly and Better Than Home Exercise for Chronic Neck Pain. *Spine (Phila Pa 1976)*. 2012;37(11):903-914. doi:10.1097/BRS.0b013e31823b3bdf
47. Ernst E. The safety of massage therapy. *Rheumatology*. 2003;42(9):1101-1106. doi:10.1093/rheumatology/keg306
48. Rendant D, Pach D, Luedtke R, et al. Qigong Versus Exercise Versus No Therapy for Patients With Chronic Neck Pain A Randomized Controlled Trial. *Spine (Phila Pa 1976)*. 2011;36(6):419-427. doi:10.1097/BRS.0b013e3181d51fca
49. Rolving N, Christiansen DH, Andersen LL, et al. Effect of strength training in addition to general exercise in the rehabilitation of patients with non-specific neck pain. A randomized clinical trial. *Eur J Phys Rehabil Med*. 2014;50(6):617-626. <http://www.ncbi.nlm.nih.gov/pubmed/24955503>.
50. Sherman KJ, Cherkin DC, Hawkes RJ, Diana L, Deyo RA. Randomized Trial of Therapeutic Massage for Chronic Neck Pain. *Clin J Pain*. 2009;25(3):233-238. doi:10.1097/AJP.0b013e31818b7912.
51. Cramer H, Lauche R, Hohmann C, et al. Randomized-controlled trial comparing yoga and home-based exercise for chronic neck pain. *Clin J Pain*. 2013;29(3):216-223. doi:10.1097/AJP.0b013e318251026c
52. Andersen LL, Saervoll CA, Mortensen OS, Poulsen OM, Hannerz H, Zebis MK. Effectiveness of small daily amounts of progressive resistance training for frequent neck/shoulder pain: Randomised controlled trial. *Pain*. 2011;152(2):440-446. doi:10.1016/j.pain.2010.11.016

53. Lilje S, Friberg H, Wykman A, Skillgate E. Naprapathic manual therapy or conventional orthopedic care for outpatients on orthopedic waiting lists?: A pragmatic randomized controlled trial. *Clin J Pain*. 2010;26(7):602-610. doi:10.1097/AJP.0b013e3181d71ebd
54. Paanalahti K, Holm LW, Nordin M, Asker M, Lyander J, Skillgate E. Adverse events after manual therapy among patients seeking care for neck and/or back pain: a randomized controlled trial. *BMC Musculoskelet Disord*. 2014;15(1):77. doi:10.1186/1471-2474-15-77
55. Lowe W. Cervical spine. In: *Orthopedic Massage*. Second. Churchill Livingstone, Inc.; 2009:199-226.
56. Sherman KJ, Dixon MW, Thompson D, Cherkin DC. Development of a taxonomy to describe massage treatments for musculoskeletal pain. *BMC Complement Altern Med*. 2006;(6). doi:10.1186/1472-6882-6-24
57. Weerapong P, Hume PA, Kolt GS. The Mechanisms of Massage and Effect on Performance, Muscle Recovery and Injury Prevention. *Sport Med*. 2005;35(3):235-256.
58. Haas C, Butterfield T a., Zhao Y, Zhang X, Jarjoura D, Best TM. Dose-dependency of massage-like compressive loading on recovery of active muscle properties following eccentric exercise: rabbit study with clinical relevance. *Br J Sports Med*. 2012;(2):83-88. doi:10.1136/bjsports-2012-091211
59. Nijs J, Kosek E, Vanoosterwijck J, et al. Dysfunctional endogenous analgesia during exercise in patients with chronic pain: to exercise or not to exercise? *Pain Physician*. 2012;15(3 Suppl):ES205-13. doi:15:ES205-ES213
60. Daenen L, Varkey E, Kellmann M, Nijs J. Exercise, not to exercise, or how to exercise in patients with chronic pain? Applying science to practice. *Clin J Pain*. 2015;31(2):108-114. doi:10.1097/AJP.0000000000000099
61. Schomacher J, Falla D. Function and structure of the deep cervical extensor muscles inpatients with neck pain. *Man Ther*. 2013;18(5):360-366. doi:10.1016/j.math.2013.05.009
62. Arimi SA, Bandpei MAM, Javanshir K, Rezasoltani A, Biglarian A. The Effect of Different Exercise Programs on Size and Function of Deep Cervical Flexor Muscles in Patients With Chronic Nonspecific Neck Pain...A Systematic Review of Randomized Controlled Trials. *Am J Phys Med Rehabil*. 2017;96(8):582-588. doi:10.1097/PHM.0000000000000721
63. Liddle SD, Gracey JH, Baxter GD. Advice for the management of low back pain : A systematic review of randomised controlled trials. *Man Ther*. 2007;12:310-327. doi:10.1016/j.math.2006.12.009
64. Skillgate E, Pico-Espinosa OJ, Côté P, et al. Effectiveness of deep tissue massage therapy, and supervised strengthening and stretching exercises for subacute or persistent disabling neck pain. The Stockholm Neck (STONE) randomized controlled trial. *Musculoskelet Sci Pract*. 2020;45:102070. doi:https://doi.org/10.1016/j.msksp.2019.102070
65. Karjalainen K, Malmivaara A, van Tulder MW, et al. Multidisciplinary biopsychosocial rehabilitation for neck and shoulder pain among working age adults

(Review). *Cochrane Database Syst Rev.* 2003;(2):2-4.
doi:10.1002/14651858.CD002194

66. Gross A, Langevin P, Burnie SJ, et al. Manipulation and mobilisation for neck pain contrasted against an inactive control or another active treatment. *Cochrane Database Syst Rev.* 2015;2015(9):CD004249. doi:10.1002/14651858.CD004249.pub4
67. ExorLive. <https://www.exorlive.com/se>.
68. Von Korff M, Ormel J, Keefe F, Dworkin S. Grading the Severity of Chronic Pain. *Pain.* 1992;50(September):133-149. doi:10.1016/0304-3959(92)90154-4
69. van der Windt DAWM, Koes BW, Boeke AJP, Jong BA De, Bouter LM. Effectiveness of corticosteroid injections versus physiotherapy for treatment of painful stiff shoulder in primary care: randomised trial. *BMJ.* 1998;317(November):1292-1296.
70. Group TE. EuroQol * - a new facility for the measurement of health-related quality of life. 1990;16:199-206.
71. Burström K, Sun S, Gerdtham UG, et al. Swedish experience-based value sets for EQ-5D health states. *Qual Life Res.* 2014;23(2):431-442. doi:10.1007/s11136-013-0496-4
72. Sweden S. SSK Standard för svensk yrkeklassificering 2012. *MIS 2012*.
73. Karasek R, Brisson C, Kawakami N, Houtman I, Bongers P, Amick B. The Job Content Questionnaire (JCQ): an instrument for internationally comparative assessments of psychosocial job characteristics. *J Occup Health Psychol.* 1998;3(4):322-355. doi:10.1037/1076-8998.3.4.322
74. World Health Organization. Body Mass Index - BMI.
75. Zigmond a S, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand.* 1983;67(6):361-370. doi:10.1111/j.1600-0447.1983.tb09716.x
76. Jung T, Wickrama KAS. An Introduction to Latent Class Growth Analysis and Growth Mixture Modeling. 2008;1:302-317.
77. Assmann SF, Pocock SJ, Enos LE, Kasten LE. Subgroup analysis and other (mis)uses of baseline data in clinical trials. *Lancet.* 2000;355(9209):1064-1069. doi:10.1016/S0140-6736(00)02039-0
78. Twisk J, Hoekstra T. Classifying developmental trajectories over time should be done with great caution: A comparison between methods. *J Clin Epidemiol.* 2012;65(10):1078-1087. doi:10.1016/j.jclinepi.2012.04.010
79. Twisk JWR. *Applied Longitudinal Data Analysis for Epidemiologists*. Second edi. Cambridge: Cambridge; 2013.
80. Proust-Lima C, Philipps V, Diakite A, Lique B. Extended Mixed Models Using Latent Classes and Latent Processes. *CRAN.* 2017.
81. Kamper SJ, Ostelo RWJG, Knol DL, Maher CG, Vet HCW De, Hancock MJ. Global Perceived Effect scales provided reliable assessments of health transition in people with musculoskeletal disorders , but ratings are strongly influenced by current status. *J Clin Epidemiol.* 2010;63(7):760-766.e1. doi:10.1016/j.jclinepi.2009.09.009

82. Dworkin RH, Turk D c, Farrar JT, et al. Core outcome measures for chronic pain clinical trials: IMMPACT recommendations. *Pain*. 2005;113(1-2):9-19.
83. Cheng YH, Huang GC. Efficacy of massage therapy on pain and dysfunction in patients with neck pain: a systematic review and meta-analysis. *Evid Based Complement Alternat Med*. 2014;2014(December 2012):204360. doi:10.1155/2014/204360
84. Ludvigsson ML, Peterson G, O’Leary S, Dederer Å, Peolsson A. The effect of neck-specific exercise with, or without a behavioral approach, on pain, disability, and self-efficacy in chronic whiplash-associated disorders: a randomized clinical trial. *Clin J Pain*. 2015;31(4):294-303. doi:10.1097/AJP.000000000000123
85. Ylinen J, Takala E-P, Nykänen M, et al. Active Neck Muscle Training in the Treatment of Chronic Neck Pain in Women. *Jama*. 2003;289(19):2509. doi:10.1001/jama.289.19.2509
86. Celenay ST, Kaya DO, Akbayrak T, et al. Cervical and scapulothoracic stabilization exercises with and without connective tissue massage for chronic mechanical neck pain: A prospective, randomised controlled trial. *Man Ther*. 2016;21:144-150. doi:10.1016/j.math.2015.07.003
87. Skillgate E, Bill A-S, Côté P, Viklund P, Peterson A, Holm LW. The effect of massage therapy and/or exercise therapy on subacute or long-lasting neck pain - the Stockholm neck trial (STONE): Study protocol for a randomized controlled trial. *Trials*. 2015;16(1). doi:http://dx.doi.org/10.1186/s13063-015-0926-4
88. Hernán MA, Robins JM. Per-Protocol Analyses of Pragmatic Trials Miguel. *N Engl J Med*. 2017;377(14):1391-1398. doi:10.1056/NEJMs1210043
89. Bothwell LE, Greene JA, Podolsky SH, Jones DS. Assessing the Gold Standard — Lessons from the History of RCTs. *N Engl J Med*. 2016;374(22):2175-2181.
90. Ablon JS, Jones EE. Validity of controlled clinical trials of psychotherapy: Findings from the NIMH treatment of depression collaborative research program. *Am J Psychiatry*. 2002;159(5):775-783. doi:10.1176/appi.ajp.159.5.775
91. Moore RA, Derry S, Wiffen PJ. Challenges in design and interpretation of chronic pain trials. *Br J Anaesth*. 2013;111(1):38-45. doi:10.1093/bja/aet126
92. Kahan BC, Rehal S, Cro S. Risk of selection bias in randomised trials. *Trials*. 2015;16(1):1-7. doi:10.1186/s13063-015-0920-x
93. Stoney CM, Lee Johnson L. *Design of Clinical Studies and Trials*. Third Edit. Elsevier Inc.; 2012. doi:10.1016/B978-0-12-382167-6.00019-9
94. Kahan BC, Doré CJ, Murphy MF, Jairath V. Bias was reduced in an open-label trial through the removal of subjective elements from the outcome definition. *J Clin Epidemiol*. 2016;77:38-43. doi:10.1016/j.jclinepi.2016.05.008
95. Kahan BC, Cro S, Doré CJ, et al. Reducing bias in open-label trials where blinded outcome assessment is not feasible: Strategies from two randomised trials. *Trials*. 2014;15(1):1-6. doi:10.1186/1745-6215-15-456
96. Salaffi F, Sarzi-puttini P, Atzeni F. How to measure chronic pain : New concepts. *Best Pract Res Clin Rheumatol*. 2015;29. doi:10.1016/j.berh.2015.04.023

97. Pool JJM, Ostelo RWJG, Hoving JL, Bouter LM, de Vet HCW. Minimal Clinically Important Change of the Neck Disability Index and the Numerical Rating Scale for Patients With Neck Pain. *Spine (Phila Pa 1976)*. 2007;32(26):3047-3051. doi:10.1097/BRS.0b013e31815cf75b
98. Kovacs FM, Abaira V, Royuela A, et al. Minimum detectable and minimal clinically important changes for pain in patients with nonspecific neck pain. *BMC Musculoskelet Disord*. 2008;9(Mdc):43. doi:10.1186/1471-2474-9-43
99. Cherkin DC, Sherman KJ, Balderson BH, et al. Effect of mindfulness-based stress reduction vs cognitive behavioral therapy or usual care on back pain and functional limitations in adults with chronic low back pain: A randomized clinical trial. *JAMA - J Am Med Assoc*. 2016;315(12):1240-1249. doi:10.1001/jama.2016.2323
100. Turner JA, Franklin G, Heagerty PJ, et al. The association between pain and disability. *Pain*. 2004;112(3):307-314. doi:10.1016/j.pain.2004.09.010
101. Skillgate E, Vingård E, Alfredsson L. Naprapathic manual therapy or evidence-based care for back and neck pain: a randomized, controlled trial. *Clin J Pain*. 2007;23(5):431-439. doi:10.1097/AJP.0b013e31805593d8
102. Payakachat N, Ali MM, Tilford JM. Can The EQ-5D Detect Meaningful Change? A Systematic Review. *Pharmacoeconomics*. 2015;33(11):1137-1154. doi:10.1007/s40273-015-0295-6.Can
103. Coretti S, Ruggeri M, McNamee P. The minimum clinically important difference for EQ-5D index: A critical review. *Expert Rev Pharmacoeconomics Outcomes Res*. 2014;14(2):221-233. doi:10.1586/14737167.2014.894462
104. Fregni F, Imamura M, Chien HF, et al. Challenges and Recommendations for Placebo Controls in Randomized Trials in Physical and Rehabilitation Medicine: A Report of the International Placebo Symposium Working Group. *Am J Phys Med Rehabil*. 2010;89(2):160-172. doi:10.1097/PHM.0b013e3181bc0bbd.Challenges
105. Hróbjartsson A, Gøtzsche PC. Is the Placebo Powerless ? An Analysis of Clinical Trials Comparing Placebo with No Treatment. *Journal, New Engl*. 2001;344(21):1594-1602.
106. McCambridge J, Sorhaindo A, Quirk A, Nanchahal K. Patient preferences and performance bias in a weight loss trial with a usual care arm. *Patient Educ Couns*. 2014;95(2):243-247. doi:10.1016/j.pec.2014.01.003
107. Bell ML, Kenward MG, Fairclough DL, Horton NJ. Differential dropout and bias in randomised controlled trials: when it matters and when it may not. *BMJ*. 2013;346:e8668. doi:10.1136/bmj.e8668
108. Higgins JP, Green S. Assessing risk of bias in included studies. In: *Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0*. The cochrane collaboration; 2011. www.handbook.cochrane.org.
109. Loudon K, Treweek S, Sullivan F, Donnan P, Thorpe KE, Zwarenstein M. The PRECIS-2 tool: Designing trials that are fit for purpose. *BMJ*. 2015;350. doi:10.1136/bmj.h2147
110. Myers M, Cairns J, Singer J. The consent form as a possible cause of side effects. 1987:250-253.

111. Bogduk N. The Neck and Headaches. *Neurol Clin NA*. 2014;32(2):471-487. doi:10.1016/j.ncl.2013.11.005
112. Boyd CM, Singh S, Varadhan R, Weiss CO, Sharma R, Bass EB PM. *Methods Research Report. Methods for Benefit and Harm Assessment in Systematic Reviews*; 2012.
113. Laupacis A, Sackett DL, Roberts RS. An assessment of clinically useful measures of the consequences of treatment. *N Engl J Med*. 1988;318(26):1728-1733.
114. Citrome L, Ketter TA. When does a difference make a difference? Interpretation of number needed to treat, number needed to harm, and likelihood to be helped or harmed. *Int J Clin Pract*. 2013;67(5):407-411. doi:10.1111/ijcp.12142
115. O'Sullivan AK, Thompson D, Drummond MF. Collection of health-economic data alongside clinical trials: Is there a future for piggyback evaluations? *Value Heal*. 2005;8(1):67-79. doi:10.1111/j.1524-4733.2005.03065.x
116. Lynöe N, Juth N. *Medicinska Etikens ABZ*. (Liber, ed.). Stockholm; 2009.
117. Ulrich CM, Wallen GR, Feister A, Grady C. Respondent burden in clinical research: When are we asking too much of subjects? *IRB Ethics Hum Res*. 2005;27(4):17-20.
118. Evans M, Robling M, Rapport FM, Houston H, Kinnersley P, Wilkinson C. It doesn't cost anything just to ask, does it? The ethics of questionnaire-based research. *J Med Ethics*. 2002;28(1):41-44. doi:10.1136/jme.28.1.41
119. Carduff E, Murray SA, Kendall M. Methodological developments in qualitative longitudinal research: The advantages and challenges of regular telephone contact with participants in a qualitative longitudinal interview study. *BMC Res Notes*. 2015;8(1):1-10. doi:10.1186/s13104-015-1107-y
120. Broderick JE, Vikingstad G. Frequent assessment of negative symptoms does not induce depressed mood. *J Clin Psychol Med Settings*. 2008;15(4):296-300. doi:10.1007/s10880-008-9127-6
121. 1177 Vårdguiden. Kiropraktik och Naprapati. Behandlingar. <https://www.1177.se/Stockholm/Fakta-och-rad/Behandlingar/Kiropraktik-och-naprapati/>. Published 2016. Accessed May 19, 2017.
122. 1177 Vårdguiden. Fysioterapi vid besvär i nacke, axlar och rygg. Behandlingar. <https://www.1177.se/Stockholm/Fakta-och-rad/Behandlingar/Sjukgymnastik-vid-besvar-i-nacke-axlar-och-rygg/>. Published 2017. Accessed April 4, 2018.
123. Dijkers MF, Westerman MJ, Rubinstein SM, Van Tulder MW, Anema JR. Why neck pain patients are not referred to manual therapy: A qualitative study among Dutch primary care stakeholders. *PLoS One*. 2016;11(6):1-18. doi:10.1371/journal.pone.0157465
124. Carey TS, Freburger JK, Holmes GM, Knauer S, Wallace A, Darter J. Race, care seeking and utilization for chronic back and neck pain: population perspectives. *J Pain*. 2011;11(4):343-350. doi:10.1016/j.jpain.2009.08.003.Race
125. Acuna SA, Chesney TR, Baxter NN. Incorporating Patient Preferences in Noninferiority Trials. *JAMA*. 2019;322(4):305-306. doi:10.1001/jama.2019.7059

12 APPENDICES

Baseline questionnaire A

Baseline questionnaire A

Baseline questionnaire B

Questionnaire on adverse events

Follow-up questionnaire at 7 weeks

Follow-up questionnaire at 3 months

Follow-up questionnaire at 6 months

Follow-up questionnaire at 1 year



**Effekten av massage och/eller träning vid långvarig nacksmärta.
En randomiserad kontrollerad studie**

1. Datum första kontakt:

2. Namn: _____

3. Telefonnummer: _____

4. Mailadress: _____

5. Hur fick du info om studien?

6. Datum för ifyllande av resterande del av enkät och Baslinje A om annat än 1:

7. Har du haft ont i nacken minst 30 dagar i sträck? (Om patienten exv svarar: Ja i 30 dagar men inte precis varenda dag, Fråga då: *Hur många dagar har du varit besvärsfri?* Om max 2 dagar i sträck – OK att vara med)

☐

JA

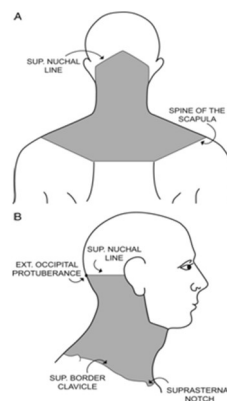
☐

NEJ

8. Har du ont i nacken idag (nacken = grått område i bild)?
(Besvären skall finnas där under någon period under dagen och ha gjort så minst en månad. Man kan vara med även om man DESSUTOM har smärta mellan skulderbladen, i bröstkorgen, utstrålning i övre extremiteter och huvudvärk. I nacksmärta inkluderas också ont i nacke efter Whiplash)

☐ JA

☐ NEJ



9. Har du eller har du haft cancersjukdom inom de senaste 5 åren?

☐ JA

☐ NEJ

10. Har du smartphone och tillgång till internet (behövs för att i vissa interventioner filma dina övningar)

☐ JA

☐ NEJ

11. Talar personen svenska tillräckligt bra för att kunna fylla i enkäterna?

☐ JA

☐ NEJ

12. Hur gammal är du? (OK 18-70 år) _____ år

13. Har du feber? (om JA: Be dem återkomma när friska)

☐ JA

☐ NEJ

14. Är du gravid?

☐

JA
relevant

☐

NEJ

☐

Inte

15. Har du varit på behandling hos massör, naprapat, kiropraktor, sjukgymnast eller osteopat för dina nackbesvär senaste månaden? (Enbart akupunktur OK)

☐ JA☐

NEJ

16. Har du gått på specifik träning för dina nackbesvär den senaste månaden?

☐ JA☐

NEJ

17. Har du hudbesvär som gör att det inte är lämpligt att ge massage i området?

☐

JA

☐

NEJ

18. Har du nyligen (inom 48 h) råkat ut för något trauma mot nacken, typ whiplash?

☐

JA

☐

NEJ

19. Är du sjukskriven på grund av planerade eller genomförda nackkirurgiska ingrepp?

☐ JA☐

NEJ

von Korff

20. På frågorna nedan skall du svara på hur stark/intensiv din smärta eller värk i **nacken** är genom att ange en siffra på en skala mellan 0 – 10, där 0 = ingen smärta/värk alls och 10 = värsta tänkbara smärta/värk. (Markera den siffra du tycker stämmer bäst)

a) Hur stark bedömer du att din smärta eller värk i **nacken** är **för tillfället**?

☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐

0 1 2 3 4 5 6 7 8 9 10

Ingen

Värsta

smärta

tänkbara smärta

b) Hur intensiv har din **värsta** smärta/värk i **nacken** varit **de senaste fyra veckorna**?

☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐

0 1 2 3 4 5 6 7 8 9 10

Ingen

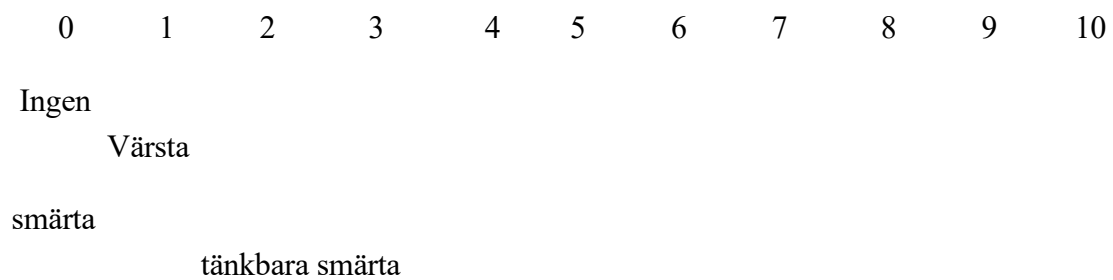
Värsta

smärta

tänkbara smärta

c) Hur intensiv har din smärta/värk varit i **nacken** i **genomsnitt de senaste fyra veckorna**?
(Med det menas hur smärtan/värken vanligtvis varit när du haft smärta)

☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐



Frågor om funktion

21. Under hur många dagar **de senaste fyra veckorna** har du inte kunnat utföra dina normala aktiviteter

(arbete, studier och/eller hushållsarbete) på grund av smärta eller värk i **nacken**?

a) Antal dagar:..... (Antal 0-30)

Besvara frågorna nedan genom att ange den siffra du tycker stämmer bäst.

b) Hur mycket har smärta eller värk i **nacken** hindrat dig i dina dagliga aktiviteter **de senaste fyra veckorna**?

<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
0	1	2	3	4	5	6	7	8	9	10
Inte alls			Omöjligt att utföra					dessa		
aktiviteter										

c) Hur mycket har smärta eller värk i **nacken** hindrat dig att ta del i fritidsaktiviteter, sociala aktiviteter och familjeaktiviteter **de senaste fyra veckorna**?

<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
0	1	2	3	4	5	6	7	8	9	10
Inte alls			Omöjligt att utföra					dessa		
aktiviteter										

d) Hur mycket har smärtan/besvären i **nacken** hindrat dig att arbeta, (inkluderat studier/hemarbete) **de senaste fyra veckorna**?

<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
0	1	2	3	4	5	6	7	8	9	10
Inte alls			Omöjligt att utföra							

Tolkning av fråga 20a)

Om de frågar så kan man tolka hur ont ”för tillfället” som hur ont idag.

Om patienten svarar: Inte just nu men i morse och andra mornar sedan en tid – fråga då: *hur mycket smärta har du då?*

Om patienten svarar: Inte just nu med det kommer att krypa på under eftermiddagen/kvällen och det har gjort så sedan en tid - Fråga då: *hur mycket smärta hade du igår?*

22. Har du under de senaste 6 månaderna haft ont i nedre delen av ryggen?

☐ Nej ☐ Ja, ett par d per månad eller mer sällan ☐ Ja, ett par d per vecka eller oftare

23. Om patienten exkluderas enligt något av ovanstående kriterier: Notera exklusionsnummer/bokstav enligt speciell lista.

24. Enkäten ifylld av:

BASELINE A



1. LÖPNUMMER

A. Namn _____

B. Personnummer:

C. Mobil nummer

D. E-postadress: _____

E. Gatuadress: _____

F. Postadress: _____

2. Jag har fått muntlig information om studien och accepterar att delta i den: ☐ Ja ☐ Nej

3. Kön: Man ☐ Kvinna ☐

4. Vem delar du bostad med? (*det vill säga vem bor du tillsammans med större delen av veckan*)? Flera alternativ kan markeras.

☐ Ingen

☐

Föräldrar/syskon

☐ Make/maka/sambo/partner

☐ Andra vuxna

☐ Barn

5. Vilken är din högsta skolutbildning?

☐ Grundskola (1-9 år)

☐ Gymnasieskola/yrkesskola (10-12 år)

☐ Universitet/högskoleutbildning (13 -15 år)

☐ Högre akademisk utbildning (16 år eller mer)

Frågor om besvären i nacke

6. På frågorna nedan ska du svara på hur stark/intensiv din smärta eller värk i nacke är, genom att ange en siffra på en skala mellan 0 – 10, där 0 = ingen smärta/värk alls och 10 = värsta tänkbara smärta/värk (*Markera den siffra du tycker stämmer bäst*)

a) Hur stark bedömer du att din smärta eller värk i nacken är **för tillfället**?

<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
0	1	2	3	4	5	6	7	8	9	10
Ingen										Värsta
smärta										tänkbara smärta

b) Hur intensiv har din **värsta** smärta/värk i nacken varit **de senaste 4 veckorna**?

<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
0	1	2	3	4	5	6	7	8	9	10

Ingen

Värsta

smärta

tänkbara smärta

c) Hur intensiv har din smärta/värk varit i nacken i **genomsnitt de senaste 4 veckorna**? (*Med det menas hur smärtan/värken vanligtvis varit när du haft smärta*)

☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐

0 1 2 3 4 5 6 7 8 9 10

Ingen

Värsta

smärta

tänkbara smärta

7. Under hur många dagar **de senaste 4 veckorna** har du **inte** kunnat utföra dina normala aktiviteter (arbete, studier och/eller hushållsarbete) på grund av smärta eller värk i nacken?

a) Antal dagar: _____

Besvara frågorna nedan genom att ange den siffra du tycker stämmer bäst.

b) Hur mycket har smärta eller värk i nacken hindrat dig i dina dagliga aktiviteter/göromål **de senaste 4 veckorna**?

☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐

0 1 2 3 4 5 6 7 8 9 10

Inte alls

Omöjligt att

utföra

dess

aktiviteter

- c) Hur mycket har smärta eller värk i nacken hindrat dig att ta del i fritidsaktiviteter, sociala aktiviteter och familjeaktiviteter **de senaste 4 veckorna?**

☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐

0 1 2 3 4 5 6 7 8 9 10

Inte alls
utföra

Omöjligt att

dessas aktiviteter

- d) Hur mycket har smärtan/besvären i nacken hindrat dig att arbeta, (inkluderat studier/hemarbete) **de senaste 4 veckorna?**

☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐

0 1 2 3 4 5 6 7 8 9 10

Inte alls
utföra

Omöjligt att

dessas

aktiviteter

8. Har du haft perioder av liknande besvär förut?

☐

Nej

☐

Ja

- 8a) Om Ja: vid _____ tillfällen (antal)

9. Hur länge har besvären pågått denna gång?

☐

1-3 månader

☐

4-6 månader

☐

7-12 månader

☐

mer än 12

månader

10. Hur började besvären denna gång?

☐

Plötsligt påkommande efter lättare belastning/våld (t.ex. hastig rörelse)

☐

Plötsligt påkommande efter tyngre belastning/våld (t.ex. fallolycka eller tungt lyft)

☐

Smygande debut under flera dagar

☐

Smygande debut under flera veckor

☐

Vet ej

11. Har du någon gång tränat med personlig tränare?

☐

Nej

☐

Ja, vid enstaka tillfällen

☐

Ja, vid flertal tillfällen

12. Har du någon gång fått massagebehandling?

☐

Ja, vid enstaka tillfällen

☐

Ja, vid flertal tillfällen

☐

Nej



ENKÄTENS FÖRSTA SIDA FYLLS I AV TERAPEUTEN

A. DAGENS DATUM

B. LÖPNUMMER

C. ☐ EXKLUDERAD PÅ GRUND AV
(KRITERIENUMMER)_____

D. ☐ 1. INKLUDERAD MASS (MASSAGE)

☐ 2. INKLUDERAD FYS (FYSISK TRÄNING)

☐ 3. INKLUDERAD MASFYS (MASSAGE OCH FYSISK TRÄNING)

☐ 4. INKLUDERAD RÅDGIV (RÅDGIVNING)

E. Vilken betydelse tror du att den behandling/träning/rådgivning du kommer att få har för tillfrisknandet? (Markera den siffra du tycker stämmer bäst)

☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐

0 1 2 3 4 5 6 7 8 9 10

Ingen betydelse
avgörande

Helt



**Karolinska
Institutet**

FYLLS I AV STUDIEDELTAGAREN

Namn:.....
....

Personnummer:.....
.....

1. Enligt din bedömning hur sannolikt är det att du är **helt besvärsfri i nacken om 7 veckor?** (Markera den siffra du tycker stämmer bäst)

☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐

0 1 2 3 4 5 6 7 8 9 10

Inte alls sannolikt

Mycket sannolikt att

att jag är helt besvärsfri

jag är helt besvärsfri

Frågor om arbete

2. Vad är din huvudsakliga sysselsättning?

- ☐ Yrkesarbetande/egenföretagare
- ☐ Arbetssökande
- ☐ Studerande
- ☐ Ålderspensionär

☐ Annat

3. Vad har du för yrke/yrkesbefattning? (Försök precisera genom att lämna en yrkesbenämning som beskriver din roll på arbetsplatsen, tex lärare i grundskola. Om frågan inte är aktuell – skriv det)

.....
.....

4. Har du tillräckligt med tid för att hinna med dina arbetsuppgifter?

☐ Ja, oftast alltid ☐ Ja ibland ☐ Nej, sällan ☐ Nej aldrig ☐ Inte aktuellt

5. Förekommer motstridiga krav i ditt arbete?

☐ Ja, oftast alltid ☐ Ja ibland ☐ Nej, sällan ☐ Nej aldrig ☐ Inte aktuellt

6. Har du frihet att bestämma **vad** som ska utföras i ditt arbete?

☐ Ja, oftast alltid ☐ Ja ibland ☐ Nej, sällan ☐ Nej aldrig ☐ Inte aktuellt

7. Har du frihet att bestämma **hur** ditt arbete ska utföras?

☐ Ja, oftast alltid ☐ Ja ibland ☐ Nej, sällan ☐ Nej aldrig ☐ Inte aktuellt

8. Hur mycket har du rört dig eller ansträngt dig kroppsligt i ditt arbete **de senaste 6 månaderna**?

☐ Stillasittande (Du har ett övervägande stillasittande arbete)

☐ Lätt men rörligt arbete (Du har ett arbete där du går ganska mycket men bär eller lyfter ☐unga saker)

Måttligt tungt arbete (Du går mycket och lyfter dessutom ganska mycket eller går uppför trappor eller i backar)

☐ Tungt arbete (Du har ett tungt kroppsarbete, lyfter tunga föremål och anstränger dig mycket kroppsligt)

☐ Inte aktuellt

9. Hur många arbetsdagar har du varit hemma från arbetet/studierna på grund av besvär i nacken **de senaste 6 månaderna**? (*Ange antal eller svara "Inte aktuellt"*)

.....

Frågor om livsstil med mera

10. Röker du dagligen?

☐

Nej

☐

Ja

11. Hur mycket väger du? kg i *heltal*

12. Hur lång är du?..... cm i *heltal*

13. *Följande frågor handlar om i vilken utsträckning du ägnar dig avsiktligt åt motions-, idrotts- eller friluftsverksamhet. OBS! Gäller fritiden och du får endast räkna med det som överstiger 20 minuters aktivitet per gång.*

Hur ofta motionerar du vanligtvis på nedanstående aktivitetsnivåer?

(Markera ett alternativ för varje aktivitetsnivå)

a) Hård ansträngningsnivå (*Du har hög puls och blir ansträngd och svettig*)

☐

Aldrig

☐

Oregelbundet

☐

En gång per vecka

☐

Två gånger per vecka

☐

Tre gånger per vecka eller oftare

b) Medelhög ansträngningsnivå (*Ansträngningsnivån ska vara sådan att det hjälpligt skulle gå att föra ett samtal med någon*)

☐

Aldrig

☐

Oregelbundet

- ☐ En gång per vecka
- ☐ Två gånger per vecka
- ☐ Tre gånger per vecka eller oftare

c) Låg ansträngningsnivå (*t.ex. lugna promenader och cykelturer*)

- ☐ Aldrig
- ☐ Oregelbundet
- ☐ En gång per vecka
- ☐ Två gånger per vecka
- ☐ Tre gånger per vecka eller oftare

14. Följande frågor handlar om sömn och återhämtning

a) Har du svårt att somna?

- ☐ Aldrig
- ☐ Sällan, några gånger per år
- ☐ Någon/några gånger per månad
- ☐ Flera gånger i veckan
- ☐ Alltid, varje dag

b) Vaknar du flera gånger på natten och har ibland svårt att somna om?

- ☐ Aldrig
- ☐ Sällan, några gånger per år
- ☐ Någon/några gånger per månad
- ☐ Flera gånger i veckan
- ☐ Alltid, varje dag

c) Känner du dig mycket trött under arbetsdagen/arbetspasset/dagliga aktiviteter?

- ☐ Aldrig
- ☐ Sällan, några gånger per år
- ☐ Någon/några gånger per månad
- ☐

Flera gånger i veckan

☐ Alltid, varje dag

Frågor om ditt humör och om dina tankar

15. Läs varje påstående och sätt ett kryss i rutan till vänster om det svar som bäst beskriver hur du känt dig under den senaste veckan. Fundera inte alltför länge. Det första svar som dyker upp är antagligen riktigare än ett svar som du funderat på länge. Svara på alla frågorna (a-g). Kryssa bara i en ruta för varje påstående.

a) Jag uppskattar fortfarande samma saker som förut

☐ Precis lika mycket

☐ Inte riktigt lika mycket

☐ Bara lite

☐ Nästan inte alls

b) Jag kan skratta och se saker från den humoristiska sidan

☐ Lika mycket som jag alltid har kunnat

☐ Inte riktigt lika mycket som förut

☐

Absolut inte lika mycket som förut

☐

Inte alls

c) Jag känner mig glad

☐

Inte alls

☐

Inte så ofta

☐

Ibland

☐

För det mesta

d) Jag känner mig som om allting går trögt

☐

Nästan jämt

☐

Ofta

☐

Ibland

☐

Inte alls

e) Jag har tappat intresset för mitt utseende

☐

Helt och hållet

☐

En hel del

☐

Inte så mycket

☐

Inte alls

f) Jag ser fram emot saker med glädje

☐ Lika mycket som jag alltid har gjort

☐ Något mindre än jag brukar

☐

Klart mindre än jag brukar

☐

Nästan inte alls

g) Jag kan njuta av en god bok, eller ett bra radio- eller TV-program

☐ Ofta

☐

Ibland

☐

Inte så ofta

☐ Mycket sällan

Frågor om vård och läkemedel för besvären i nacken

16. Redovisa nedan vilken vård/behandling du har sökt för besvär i nacken **de senaste 6 månaderna**.

a) Sjukgymnast

☐

Nej

☐

Ja - antal besök.....

b) Naprapat

☐

Nej

☐

Ja - antal besök.....

c) Kiropraktor

☐

Nej

☐

Ja - antal besök.....

d) Osteopat

☐

Nej

☐

Ja - antal besök

e) Massör

☐

Nej

☐

Ja - antal besök.....

f) Läkare

☐

Nej

☐

Ja - antal besök.....

g) Annat

☐

Nej

☐

Ja - antal besök.....

Om ja

vad?.....

h) Annat

☐

Nej

☐

Ja- antal besök.....

Om ja
vad?.....

16 i) Utredning i form av röntgen eller liknande?

☐

Nej

☐

Ja- antal besök

Om ja
vad?.....

17. Vilket läkemedel/naturläkemedel och hur ofta har du konsumerat som direkt följd av besvären i

nacken **de senaste 6 månaderna?**

a) Naturläkemedel

☐

Aldrig

☐

Ja, ibland

☐

Ja, dagligen

Om ja, vilket/vilka?

.....
.....

b) Receptfria läkemedel

☐

Aldrig

☐

Ja, ibland

☐

Ja, dagligen

Om ja, vilket/vilka?

.....
.....

c) Receptbelagda läkemedel

☐ Aldrig ☐ Ja, ibland ☐ Ja, dagligen

Om ja, vilket/vilka?

.....
.....

Frågor om din hälsa

18. I allmänhet, skulle du vilja säga att din hälsa är?

Utmärkt Mycket god God Någorlunda Dålig
☐ ☐ ☐ ☐ ☐

19. Har du av läkare fått någon eller några av följande diagnoser?

a) Diabetes

☐ Har ☐ Har haft ☐ Har aldrig haft

b) Astma

☐ Har ☐ Har haft ☐ Har aldrig haft

c) Kronisk obstruktiv lungsjukdom (KOL)?

☐ Har ☐ Har haft ☐ Har aldrig haft

d) Psoriasis?

☐ Har

☐ Har haft

☐ Har aldrig haft

e) Förhöjda blodfetter?

☐ Har

☐ Har haft

☐ Har aldrig haft

f) Depression?

☐ Har

☐ Har haft

☐ Har aldrig haft

g) Kronisk trötthetssyndrom, utmattningsdepression, utmattningssyndrom eller utbrändhet?

☐ Har

☐ Har haft

☐ Har aldrig haft

EQ-5D. Markera, genom att kryssa i EN ruta i varje nedanstående grupp för det påstående som bäst beskriver ditt hälsotillstånd idag

20. Rörlighet

Jag går utan svårigheter

☐

Jag kan gå med viss svårighet

☐

Jag är sängliggande

☐

21. Hygien

Jag behöver ingen hjälp med min dagliga hygien, mat eller påklädnin

☐

Jag har vissa problem att tvätta eller klä mig själv

☐

Jag kan inte tvätta eller klä mig själv

☐

22. Huvudsakliga aktiviteter

(t ex arbete, studier, hushållssysslor, familje- och fritidsaktiviteter)

Jag klarar av mina huvudsakliga aktiviteter

☐

Jag har vissa problem med att utföra mina huvudsakliga aktiviteter

☐

Jag klarar inte av mina huvudsakliga aktiviteter

☐

23. Smärtor eller besvär

Jag har varken smärtor eller besvär

☐

Jag har måttliga smärtor eller besvär

☐

Jag har svåra smärtor eller besvär

☐

24. Oro/nedstämdhet

Jag är inte orolig eller nedstämd

☐

Jag är orolig eller nedstämd

☐

Jag är i högsta grad orolig eller nedstämd

☐

© EuroQol Group 1990



FRÅGOR OM BEHANDLINGSREAKTIONER

A. DAGENS DATUM

NAMN _____

PERSONNUMMER _____

B. Enkäten fylldes i vid besökstillfälle nummer:

och gäller reaktioner efter förra behandlingen.

C. Om du av terapeuten fått ett träningsprogram att göra hemma, hur många gånger har du gjort hela det programmet sedan förra behandlingstillfället? (ange antal)



Det händer att patienter upplever oönskade reaktioner i samband med behandling/träning. Därför undrar vi om du som en direkt effekt av behandlingen upplevt något av följande?

OBS! Ange endast symptom som har debuterat inom 24 timmar efter behandlingen.

1. Trötthet?

☐ Nej - Gå till fråga 2

☐ Ja

Hur länge pågick reaktionen? (timmar).....

Hur mycket besvärade det dig?

0 1 2 3 4 5 6 7 8 9 10

☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐

Inte alls
sätt

På värsta tänkbara

2. Ömhet i muskler?

☐ Nej - Gå till fråga 3

☐ Ja

Hur länge pågick behandlingsreaktionen? (timmar).....

Hur mycket besvärade det dig?

0 1 2 3 4 5 6 7 8 9 10

☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐

Inte alls
sätt

På värsta tänkbara

3. Ökad stelhet?

☐ Nej - Gå till fråga 4

☐ Ja

Hur länge pågick behandlingsreaktionen? (timmar).....

Hur mycket besvärade det dig?

0 1 2 3 4 5 6 7 8 9 10

☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐

Inte alls

På värsta tänkbara sätt

(vänd)

4. Ökad smärta?

☐ Nej - Gå till fråga 5

☐ Ja

Hur länge pågick behandlingsreaktionen? (timmar).....

Hur mycket besvärade det dig?

0 1 2 3 4 5 6 7 8 9 10

☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐

Inte alls
sätt

På värsta tänkbara

5. Ostadighet/yrsel?

☐ Nej - Gå till fråga 6

☐ Ja

Hur länge pågick behandlingsreaktionen? (timmar).....

Hur mycket besvärade det dig?

0 1 2 3 4 5 6 7 8 9 10

☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐

Inte alls
sätt

På värsta tänkbara

6. Huvudvärk?

☐ Nej - Gå till fråga 7

☐ Ja

Hur länge pågick behandlingsreaktionen? (timmar).....

Hur mycket besvärade det dig?

0 1 2 3 4 5 6 7 8 9 10

☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐

Inte alls
sätt

På värsta tänkbara

(vänd)

7. Illamående?

☐ Nej – Gå till fråga 8

☐ Ja

Hur länge pågick behandlingsreaktionen? (timmar).....

Hur mycket besvärade det dig?

0 1 2 3 4 5 6 7 8 9 10

☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐

Inte alls
sätt

På värsta tänkbara

8. Annat?

☐ Nej

☐ Ja

Specificera vad?.....

Hur länge pågick behandlingsreaktionen? (timmar).....

Hur mycket besvärade det dig?

0 1 2 3 4 5 6 7 8 9 10

☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐

Inte alls
sätt

På värsta tänkbara



Karolinska Institutet, Institutet för Miljömedicin – Vänligen fyll i formuläret

UPPFÖLJNING 7 VECKOR EFTER STUDIENS START





Frågor om besvären i nacken

1. Vilket av nedanstående påståenden stämmer bäst överens med hur du upplever att dina besvär i nacken har förändrats sedan du gick med i denna studie?

☐

Är helt smärtfri och har inte heller andra besvär från nacken

☐

Är betydligt förbättrad

☐

Är något förbättrad

☐

Ingen förändring

☐

Är något försämrad

☐

Är betydligt försämrad

2. På frågorna nedan ska du svara på hur stark/intensiv din smärta eller värk i nacken är genom att ange en siffra på en skala mellan 0 – 10, där 0 = ingen smärta/värk alls och 10 = värsta tänkbara smärta/värk. *(Markera den siffra du tycker stämmer bäst)*

d) Hur stark bedömer du att din smärta eller värk i nacken är **för tillfället**?

☐☐☐☐☐☐☐☐☐☐☐

0

1

2

3

4

5

6

7

8

9

10

Ingen

Värsta

smärta

tänkbara smärta

e) Hur intensiv har din **värsta** smärta/värk i nacken varit **de senaste fyra veckorna**?

☐☐☐☐☐☐☐☐☐☐☐

0

1

2

3

4

5

6

7

8

9

10

Ingen

Värsta

smärta

tänkbara

smärta

f) Hur intensiv har din smärta/värk varit i nacken i **genomsnitt de senaste fyra veckorna**?
(Med det menas hur smärtan/värken vanligtvis varit när du haft smärta)

☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐

0 1 2 3 4 5 6 7 8 9 10

Ingen smärta smärta smärta Värsta tänkbara

3. Under hur många dagar **de senaste fyra veckorna** har du **inte** kunnat utföra dina normala aktiviteter (arbete, studier och/eller hushållsarbete) på grund av smärta eller värk i nacken?

a) Antal dagar:.....

(Vänd)

Besvara frågorna nedan genom att ange den siffra du tycker stämmer bäst.

b) Hur mycket har smärta eller värk i nacken hindrat dig i dina dagliga aktiviteter **de senaste fyra veckorna?**

<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
0	1	2	3	4	5	6	7	8	9	10
Inte alls					Omöjligt att					
utföra					dessa					
aktiviteter										

c) Hur mycket har smärta eller värk i nacken hindrat dig att ta del i fritidsaktiviteter, sociala aktiviteter och familjeaktiviteter **de senaste fyra veckorna?**

<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
0	1	2	3	4	5	6	7	8	9	10
Inte alls					Omöjligt att					
utföra					dessa					
aktiviteter										

d) Hur mycket har smärtan/besvären i nacken hindrat dig att arbeta, (inkluderat studier/hemarbete)

de senaste fyra veckorna?

<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
0	1	2	3	4	5	6	7	8	9	10
Inte alls					Omöjligt att					
utföra										

aktiviteter

4. Överlag, hur nöjd är du med den behandling/träning/rådgivning som du fått i denna studie för dina besvär i nacken? *(Avser de behandlingar som ingick i denna studie)*

☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐

0 1 2 3 4 5 6 7 8 9 10

Inte alls nöjd

Överträffade mina

förväntningar

Frågor om hälsa

Mycket

Utmärkt god God Någorlunda

Dålig

☐ ☐ ☐ ☐ ☐

5. I allmänhet, skulle du vilja säga att din hälsa är:

EQ-5D

Markera, genom att kryssa i en ruta i varje nedanstående grupp, vilket påstående som bäst beskriver ditt hälsotillstånd idag

6. Rörlighet

Jag går utan svårigheter

☐

Jag kan gå med viss svårighet

☐

Jag är sängliggande

☐

(Vänd)

7. Hygien

Jag behöver ingen hjälp med min dagliga hygien, mat eller påklädning ☐

Jag har vissa problem att tvätta eller klä mig själv ☐

Jag kan inte tvätta eller klä mig själv ☐

8. Huvudsakliga aktiviteter (*t ex arbete, studier, hushållssysslor, familje- och fritidsaktiviteter*)

Jag klarar av mina huvudsakliga aktiviteter ☐

Jag har vissa problem med att utföra mina huvudsakliga aktiviteter ☐

Jag klarar inte av mina huvudsakliga aktiviteter ☐

9. Smärtor eller besvär

Jag har varken smärtor eller besvär ☐

Jag har måttliga smärtor eller besvär ☐

Jag har svåra smärtor eller besvär ☐

10. Oro/nedstämdhet

Jag är inte orolig eller nedstämd ☐

Jag är orolig eller nedstämd ☐

Jag är i högsta grad orolig eller nedstämd ☐

11. Termomterliknande skala

På denna sida har Ditt bästa tänkbara hälsotillstånd markerats med 100 och Ditt sämsta tänkbara hälsotillstånd med 0.

**Karolinska Institutet, Institutet för Miljömedicin – Vänligen fyll i
formuläret**

***UPPFÖLJNING 3 MÅNADER EFTER STUDIENS
START***





Frågor om besvären i nacken

1. Vilket av nedanstående påståenden stämmer bäst överens med hur du upplever att dina besvär i nacken har förändrats sedan du gick med i denna studie?

☐

Är helt smärtfri och har inte heller andra besvär från nacken

☐

Är betydligt förbättrad

☐

Är något förbättrad

☐

Ingen förändring

☐

Är något försämrad

☐

Är betydligt försämrad

2. På frågorna nedan skall du svara på hur stark/intensiv din smärta eller värk i nacken är genom att ange en siffra på en skala mellan 0 – 10, där 0 = ingen smärta/värk alls och 10 = värsta tänkbara smärta/värk. *(Markera den siffra du tycker stämmer bäst)*

- g) Hur stark bedömer du att din smärta eller värk i nacken är **för tillfället**?

☐☐☐☐☐☐☐☐☐☐☐

0

1

2

3

4

5

6

7

8

9

10

Ingen

Värsta

smärta

tänkbara smärta

- h) Hur intensiv har din **värsta** smärta/värk i nacken varit **de senaste fyra veckorna**?

☐☐☐☐☐☐☐☐☐☐☐

0

1

2

3

4

5

6

7

8

9

10

Ingen

Värsta

smärta

tänkbara

smärta

- i) Hur intensiv har din smärta/värk varit i nacken i **genomsnitt de senaste fyra veckorna**?
(Med det menas hur smärtan/värken vanligtvis varit när du haft smärta)

☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐

0 1 2 3 4 5 6 7 8 9 10

Ingen smärta smärta Värsta tänkbara smärta

3. Under hur många dagar **de senaste fyra veckorna** har du **inte** kunnat utföra dina normala aktiviteter (arbete, studier och/eller hushållsarbete) på grund av smärta eller värk i nacken?

a) Antal dagar:.....

(Vänd)

Besvara frågorna nedan genom att ange den siffra du tycker stämmer bäst.

- b) Hur mycket har smärta eller värk i nacken hindrat dig i dina dagliga aktiviteter/göromål de senaste fyra veckorna?

<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
0	1	2	3	4	5	6	7	8	9	10
Inte alls				Omöjligt att						
utföra				dessa						
aktiviteter										

- c) Hur mycket har smärta eller värk i nacken hindrat dig att ta del i fritidsaktiviteter, sociala aktiviteter och familjeaktiviteter **de senaste fyra veckorna?**

<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
0	1	2	3	4	5	6	7	8	9	10
Inte alls				Omöjligt att						
utföra				dessa						
aktiviteter										

- d) Hur mycket har smärtan/besvären i nacken hindrat dig att arbeta, (inkluderat studier/hemarbete) **de senaste fyra veckorna?**

<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
0	1	2	3	4	5	6	7	8	9	10
Inte alls				Omöjligt att						
utföra										

aktiviteter

Frågor om hälsa

4. Redovisa nedan vilken vård/ behandling du har sökt för besvär i nacken, utöver de behandlingstillfällen som ingick i studien. Uppgiften gäller endast vård/ behandling du har sökt **de senaste 3 månaderna**:

a) Sjukgymnast	<input type="checkbox"/>	Nej	<input type="checkbox"/>	Ja	- om Ja ange antal besök
_____	<input type="checkbox"/>		<input type="checkbox"/>		
b) Naprapat	<input type="checkbox"/>	Nej	<input type="checkbox"/>	Ja	- om Ja ange antal besök
_____	<input type="checkbox"/>		<input type="checkbox"/>		
c) Kiropraktor	<input type="checkbox"/>	Nej	<input type="checkbox"/>	Ja	- om Ja ange antal besök
_____	<input type="checkbox"/>		<input type="checkbox"/>		
d) Osteopat	<input type="checkbox"/>	Nej	<input type="checkbox"/>	Ja	- om Ja ange antal besök
_____	<input type="checkbox"/>		<input type="checkbox"/>		
e) Massör	<input type="checkbox"/>	Nej	<input type="checkbox"/>	Ja	- om Ja ange antal
besök _____	<input type="checkbox"/>		<input type="checkbox"/>		
f) Läkare	<input type="checkbox"/>	Nej	<input type="checkbox"/>	Ja	- om Ja ange antal
besök _____	<input type="checkbox"/>		<input type="checkbox"/>		
g) Annat		Nej		Ja	- om Ja ange antal
besök _____					
-ange vad:	_____				
h) Annat	<input type="checkbox"/>	Nej	<input type="checkbox"/>	Ja	- om Ja ange antal
besök _____					
-om Ja ange					
vad:	_____				
i) Utredning i form av röntgen el liknande					
_____	<input type="checkbox"/>	Nej	<input type="checkbox"/>	JA	om ja ange antal besök

-om Ja ange
vad: _____

(Vänd)

5. Vilka läkemedel/naturläkemedel och hur ofta har du konsumerat som direkt följd av besvären i nacken

de senaste 3 månaderna?

a) Naturläkemedel:

☐ Aldrig ☐ Ibland ☐ Dagligen

Vilket/Vilka? _____

b) Receptfria läkemedel?

☐ Aldrig ☐ Ibland ☐ Dagligen

Vilket/Vilka? _____

c) Receptbelagda läkemedel?

☐ Aldrig ☐ Ibland ☐ Dagligen

Vilket/Vilka? _____

6. Hur många **arbetsdagar** har du varit hemma från arbetet/studier pga besvär i nacken

de senaste 3 månaderna? _____ (Ange antal dagar eller svara ” Inte aktuellt” om du inte arbetar)

Mycket

	Utmärkt	god	God	Någorlunda
Dålig	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

7. I allmänhet, skulle du vilja säga att din hälsa är:

EQ-5D

Markera, genom att kryssa i en ruta i varje nedanstående grupp, det påstående som bäst beskriver ditt hälsotillstånd idag:

8. Rörlighet

Jag går utan svårigheter	<input type="checkbox"/>
Jag kan gå men med viss svårighet	<input type="checkbox"/>
Jag är sängliggande	<input type="checkbox"/>

9. Hygien

Jag behöver ingen hjälp med min dagliga hygien, mat eller påklädning	<input type="checkbox"/>
Jag har vissa problem att tvätta eller klä mig själv	<input type="checkbox"/>
Jag kan inte tvätta eller klä mig själv	<input type="checkbox"/>

10. Huvudsakliga aktiviteter (t ex arbete, studier,

hushållssysslor, familje- och fritidsaktiviteter)	
Jag klarar av mina huvudsakliga aktiviteter	<input type="checkbox"/>
Jag har vissa problem med att klara av mina vanliga aktiviteter	<input type="checkbox"/>
Jag klarar inte av mina vanliga aktiviteter	<input type="checkbox"/>

(Vänd)

11. Smärtor/besvär

Jag har varken smärtor eller besvär

☐

Jag har måttliga smärtor eller besvär

☐

Jag har svåra smärtor eller besvär

☐

12. Oro/nedstämdhet

Jag är inte orolig eller nedstämd

☐

Jag är orolig eller nedstämd i viss utsträckning

☐

Jag är i högsta grad orolig eller nedstämd

☐

11. Termomterliknande skala

På denna sida har Ditt bästa tänkbara hälsotillstånd markerats med 100 och Ditt sämsta tänkbara hälsotillstånd med 0.

**Karolinska Institutet, Institutet för Miljömedicin – Vänligen fyll i
formuläret**

***UPPFÖLJNING 6 MÅNADER EFTER STUDIENS
START***





**Karolinska
Institutet**

Frågor om besvären i nacken

1. Vilket av nedanstående påståenden stämmer bäst överens med hur du upplever att dina besvär i nacken har förändrats sedan du gick med i denna studie?

<input type="checkbox"/>	Är helt smärtfri och har inte heller andra besvär från nacken
<input type="checkbox"/>	Är betydligt förbättrad
<input type="checkbox"/>	Är något förbättrad
<input type="checkbox"/>	Ingen förändring
<input type="checkbox"/>	Är något försämrad
<input type="checkbox"/>	Är betydligt försämrad

2. På frågorna nedan skall du svara på hur stark/intensiv din smärta eller värk i nacken är genom att ange en siffra på en skala mellan 0 – 10, där 0 = ingen smärta/värk alls och 10 = värsta tänkbara smärta/värk. *(Markera den siffra du tycker stämmer bäst)*

- j) Hur stark bedömer du att din smärta eller värk i nacken är **för tillfället**?

<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
--------------------------	--------------------------	--------------------------	--------------------------	--------------------------	--------------------------	--------------------------	--------------------------	--------------------------	--------------------------	--------------------------

0 1 2 3 4 5 6 7 8 9 10

Ingen

Värsta

smärta

tänkbara smärta

- k) Hur intensiv har din **värsta** smärta/värk i nacken varit **de senaste fyra veckorna**?

<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
--------------------------	--------------------------	--------------------------	--------------------------	--------------------------	--------------------------	--------------------------	--------------------------	--------------------------	--------------------------	--------------------------

0 1 2 3 4 5 6 7 8 9 10

Ingen

Värsta

smärta

tänkbara

smärta

- l) Hur intensiv har din smärta/värk varit i nacken i **genomsnitt de senaste fyra veckorna**?
(Med det menas hur smärtan/värken vanligtvis varit när du haft smärta)

<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
0	1	2	3	4	5	6	7	8	9	10
Ingen							Värsta			
smärta							tänkbara			
smärta										

3. Under hur många dagar **de senaste fyra veckorna** har du inte kunnat utföra dina normala aktiviteter (arbete, studier och/eller hushållsarbete) på grund av smärta eller värk i nacken?

a) Antal dagar:.....

(Vänd)

Besvara frågorna nedan genom att ange den siffra du tycker stämmer bäst.

b) Hur mycket har smärta eller värk i nacken hindrat dig i dina dagliga aktiviteter **de senaste fyra veckorna**?

<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
0	1	2	3	4	5	6	7	8	9	10

Inte alls
utföra

Omöjligt att

dessa

aktiviteter

- c) Hur mycket har smärta eller värk i nacken hindrat dig att ta del i fritidsaktiviteter, sociala aktiviteter och familjeaktiviteter **de senaste fyra veckorna?**

☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐

0 1 2 3 4 5 6 7 8 9 10

Inte alls
utföra

Omöjligt att

dessa

aktiviteter

- d) Hur mycket har smärtan/besvären i **nacken** hindrat dig att arbeta, (inkluderat studier/hemarbete) **de senaste fyra veckorna?**

☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐

0 1 2 3 4 5 6 7 8 9 10

Inte alls
utföra

Omöjligt att

dessa

aktiviteter

Frågor om din hälsa

4. Redovisa nedan vilken vård/behandling du har sökt för besvär i nacken **de senaste 3 månaderna**:

_____	a) Sjukgymnast	<input type="checkbox"/>	Nej	<input type="checkbox"/>	Ja	-om Ja ange antal besök
_____	b) Naprapat	<input type="checkbox"/>	Nej	<input type="checkbox"/>	Ja	-om Ja ange antal besök
_____	c) Kiropraktor	<input type="checkbox"/>	Nej	<input type="checkbox"/>	Ja	-om Ja ange antal besök
_____	d) Osteopat	<input type="checkbox"/>	Nej	<input type="checkbox"/>	Ja	-om Ja ange antal besök
_____	e) Massör	<input type="checkbox"/>	Nej	<input type="checkbox"/>	Ja	-om Ja ange antal besök
_____	f) Läkare	<input type="checkbox"/>	Nej	<input type="checkbox"/>	Ja	-om Ja ange antal besök
_____	g) Annat		Nej		Ja	-om Ja ange antal besök
vad: _____	-om Ja ange	<input type="checkbox"/>		<input type="checkbox"/>		
_____	h) Annat		Nej		JA	-om Ja ange antal besök
vad: _____	-om Ja ange					
_____	i) Utredning i form av röntgen el liknande	<input type="checkbox"/>	Nej	<input type="checkbox"/>	JA	-om Ja ange antal besök
vad: _____	-om Ja ange					

(Vänd)

5. Vilka läkemedel/naturläkemedel och hur ofta har du konsumerat som direkt följd av besvären i nacken

de senaste 3 månaderna?

a) Naturläkemedel:

☐ Aldrig ☐ Ibland ☐ Dagligen

Vilket/vilka? _____

b) Receptfria läkemedel?

☐ Aldrig ☐ Ibland ☐ Dagligen

Vilket/vilka? _____

c) Receptbelagda läkemedel?

☐ Aldrig ☐ Ibland ☐ Dagligen

Vilke/Vilka? _____

6. Hur många **arbetsdagar** har du varit hemma från arbetet pga besvär i nacken

de senaste 3 månaderna? _____ (Ange antal dagar eller svara ” Inte aktuellt” om du inte arbetar.)

			Mycket		
			Utmärkt	god	God
			Någorlunda		
Dålig	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

7. I allmänhet, skulle du vilja säga att din hälsa är:

EQ-5D

Markera, genom att kryssa i en ruta i varje nedanstående grupp, det påstående som bäst beskriver ditt hälsotillstånd idag:

8. Rörlighet

- | | |
|-----------------------------------|--------------------------|
| Jag går utan svårigheter | <input type="checkbox"/> |
| Jag kan gå men med viss svårighet | <input type="checkbox"/> |
| Jag är sängliggande | <input type="checkbox"/> |

9. Hygien

- | | |
|----------------------------------------------------------------------|--------------------------|
| Jag behöver ingen hjälp med min dagliga hygien, mat eller påklädning | <input type="checkbox"/> |
| Jag har vissa problem att tvätta eller klä mig själv | <input type="checkbox"/> |
| Jag kan inte tvätta eller klä mig själv | <input type="checkbox"/> |

10. Huvudsakliga aktiviteter (t ex arbete, studier,

hushållssysslor, familje- och fritidsaktiviteter)

- | | |
|-----------------------------------------------------------------|--------------------------|
| Jag klarar av mina huvudsakliga aktiviteter | <input type="checkbox"/> |
| Jag har vissa problem med att klara av mina vanliga aktiviteter | <input type="checkbox"/> |
| Jag klarar inte av mina vanliga aktiviteter | <input type="checkbox"/> |

(Vänd)

11. Smärtor/besvär

- | | |
|---------------------------------------|--------------------------|
| Jag har varken smärtor eller besvär | <input type="checkbox"/> |
| Jag har måttliga smärtor eller besvär | <input type="checkbox"/> |
| Jag har svåra smärtor eller besvär | <input type="checkbox"/> |

12. Oro/nedstämdhet

Jag är inte orolig eller nedstämd

☐

Jag är orolig eller nedstämd i viss utsträckning

☐

Jag är i högsta grad orolig eller nedstämd

☐

13. Termomterliknande skala

På denna sida har Ditt bästa tänkbara hälsotillstånd markerats med 100 och Ditt sämsta tänkbara hälsotillstånd med 0.

© EuroQol Group. EQ-5D™ is a trade mark of the EuroQol Group

Karolinska Institutet, Institutet för Miljömedicin – Vänligen fyll i formuläret

***UPPFÖLJNING 12 MÅNADER EFTER STUDIENS
START***





Frågor om besvär i nacke

1. Vilket av nedanstående påståenden stämmer bäst överens med hur du upplever att dina besvär i nacken har förändrats sedan du gick med i denna studie?

<input type="checkbox"/>	Är helt smärtfri och har inte heller andra besvär från nacken
<input type="checkbox"/>	Är betydligt förbättrad
<input type="checkbox"/>	Är något förbättrad
<input type="checkbox"/>	Ingen förändring
<input type="checkbox"/>	Är något försämrad
<input type="checkbox"/>	Är betydligt försämrad

2. På frågorna nedan skall du svara på hur stark/intensiv din smärta eller värk i nacken är genom att ange en siffra på en skala mellan 0 – 10, där 0 = ingen smärta/värk alls och 10 = värsta tänkbara smärta/värk. (Markera den siffra du tycker stämmer bäst)

- m) Hur stark bedömer du att din smärta/värk i nacken är **för tillfället**?

<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
--------------------------	--------------------------	--------------------------	--------------------------	--------------------------	--------------------------	--------------------------	--------------------------	--------------------------	--------------------------	--------------------------

0 1 2 3 4 5 6 7 8 9 10

Ingen

Värsta

smärta

tänkbara smärta

- n) Hur intensiv har din **värsta** smärta/värk i nacken varit **de senaste fyra veckorna**?

<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
--------------------------	--------------------------	--------------------------	--------------------------	--------------------------	--------------------------	--------------------------	--------------------------	--------------------------	--------------------------	--------------------------

0 1 2 3 4 5 6 7 8 9 10

Ingen

Värsta

smärta
smärta

tänkbara

- o) Hur intensiv har din smärta/värk varit i **nacken** i **genomsnitt de senaste fyra veckorna**?
(Med det menas hur smärtan/värken vanligtvis varit när du haft smärta)

☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐

0 1 2 3 4 5 6 7 8 9 10

Ingen

Värsta

smärta
smärta

tänkbara

3. Under hur många dagar **de senaste fyra veckorna** har du **inte** kunnat utföra dina normala aktiviteter

(arbete, studier, och/eller hushållsarbete) på grund av smärta eller värk i nacken?

a) Antal dagar: _____

Besvara frågorna nedan genom att ange den siffra du tycker stämmer bäst

- b) Hur mycket har smärta eller värk i nacken hindrat dig i dina dagliga aktiviteter/göromål **de senaste fyra veckorna**?

☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐

0 1 2 3 4 5 6 7 8 9 10

Inte alls
utföra

Omöjligt att

aktiviteter

dess

- c) Hur mycket har smärta eller värk i nacken hindrat dig att ta del i fritidsaktiviteter, sociala aktiviteter och familjeaktiviteter **de senaste fyra veckorna**?

☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐

0 1 2 3 4 5 6 7 8 9 10

Inte alls Omöjligt att
utföra dessa
aktiviteter

- d) Hur mycket har smärtan/besvären i nacken hindrat dig att arbeta (inkluderat studier/hemarbete) **de senaste fyra veckorna**?

☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐

0 1 2 3 4 5 6 7 8 9 10

Inte alls Omöjligt att
utföra dessa
aktiviteter

Frågor om arbete

4. Vad är din huvudsakliga sysselsättning?

- ☐ Yrkesarbetande/egenföretagare
☐ Arbetssökande
☐ Studerande
☐ Ålderspensionär
☐ Annat

5. Har du tillräckligt med tid för att hinna med dina arbetsuppgifter?

☐ Ja, oftast alltid ☐ Ja ibland ☐ Nej, sällan ☐ Nej aldrig ☐ Inte aktuellt

6. Förekommer motstridiga krav i ditt arbete?

☐ Ja, oftast alltid ☐ Ja ibland ☐ Nej, sällan ☐ Nej aldrig ☐ Inte aktuellt

7. Har du frihet att bestämma **vad** som ska utföras i ditt arbete?

☐ Ja, oftast alltid ☐ Ja ibland ☐ Nej, sällan ☐ Nej aldrig ☐ Inte aktuellt

8. Har du frihet att bestämma **hur** ditt arbete ska utföras?

☐ Ja, oftast alltid ☐ Ja ibland ☐ Nej, sällan ☐ Nej aldrig ☐ Inte aktuellt

9. Hur mycket har du rört dig eller ansträngt dig kroppsligt i ditt arbete **de senaste 6 månaderna**?

☐ Stillasittande (*Du har ett övervägande stillasittande arbete*)

☐ Lätt men rörligt arbete (*Du har ett arbete där du går ganska mycket men bär eller lyfter ej tunga saker*)

☐ Måttligt tungt arbete (*Du går mycket och lyfter dessutom ganska mycket eller går uppför trappor eller i backar*)

☐ Tungt arbete (*Du har ett tungt kroppsarbete, lyfter tunga föremål och anstränger dig mycket kroppsligt*)

10. Hur många **arbetsdagar** har du varit hemma från arbetet/studier på grund av besvär i nacken

de senaste 6 månaderna? _____ (*Ange antal dagar eller svara med " Inte aktuellt "*)

Frågor om livsstil med mera

11. Följande frågor handlar om i vilken utsträckning du ägnar dig avsiktligt åt motions-, idrotts- eller friluftsverksamhet. OBS! Gäller fritiden och du får endast räkna med det som överstiger 20 minuters aktivitet per gång.

Hur ofta motionerar du vanligtvis på nedanstående aktivitetsnivåer?

(Markera ett alternativ för varje aktivitetsnivå)

a) Hård ansträngningsnivå (Du har hög puls och blir ansträngd och svettig)

- ☐ Aldrig
- ☐ Oregelbundet
- ☐ En gång per vecka
- ☐ Två gånger per vecka
- ☐ Tre gånger per vecka eller oftare

b) Medelhög ansträngningsnivå (Ansträngningsnivån ska vara sådan att det hjälpligt skulle gå att föra ett samtal med någon)

- ☐ Aldrig
- ☐ Oregelbundet
- ☐ En gång per vecka
- ☐ Två gånger per vecka
- ☐ Tre gånger per vecka eller oftare

c) Låg ansträngningsnivå (t.ex. lugna promenader och cykelturer)

- ☐ Aldrig
- ☐ Oregelbundet
- ☐ En gång per vecka
- ☐ Två gånger per vecka
- ☐ Tre gånger per vecka eller oftare

12. Har du svårt att somna?

- ☐ Aldrig
- ☐ Sällan, några gånger per år
- ☐ Någon/några gånger per månad
- ☐ Flera gånger i veckan
- ☐ Alltid, varje dag

13. Vaknar du flera gånger på natten och har ibland svårt att somna om?

- ☐ Aldrig
- ☐ Sällan, några gånger per år
- ☐ Någon/några gånger per månad
- ☐ Flera gånger i veckan
- ☐ Alltid, varje dag

14. Känner du dig mycket trött under arbetsdagen/arbetspasset/dagliga aktiviteter?

- ☐ Aldrig
 - ☐ Sällan, några gånger per år
 - ☐ Någon/några gånger per månad
 - ☐ Flera gånger i veckan
 - ☐ Alltid, varje dag
-
-

Frågor om ditt humör och om dina tankar

15. Läs varje påstående och sätt ett kryss i rutan till vänster om det svar som kommer närmast hur Du känt dig under **den senaste veckan**. Fundera inte alltför länge. Det första svar som dyker upp är antagligen riktigare än ett svar som Du funderat på länge. **Svara på alla frågorna (a-g).** Kryssa bara i **en** ruta för varje påstående.

- a) Jag uppskattar fortfarande samma saker som förut
- ☐ Precis lika mycket

☐ Inte riktigt lika mycket

☐ Bara lite

☐ Nästan inte alls

b) Jag kan skratta och se saker från den humoristiska sidan

☐

☐ Lika mycket som jag alltid har kunnat

☐

Inte riktigt lika mycket som förut

☐ Absolut inte lika mycket som förut

☐ Inte alls

c) Jag känner mig glad

☐

Inte alls

☐ Inte så ofta

☐ Ibland

☐

För det mesta

d) Jag känner mig som om allting går trögt

☐

☐ Nästan jämt

☐

Ofta

☐ Ibland

☐

Inte alls

e) Jag har tappat intresset för mitt utseende

☐

☐ Helt och hållet

En hel del

☐

Inte så mycket

☐

Inte alls

f) Jag ser fram emot saker med glädje

☐

Lika mycket som jag alltid har gjort

☐

Något mindre än jag brukar

☐

Klart mindre än jag brukar

☐

Nästan inte alls

g) Jag kan njuta av en god bok, eller ett bra radio- eller TV-program

☐

Ofta

☐

Ibland

☐

Inte så ofta

☐

Mycket Sällan

Frågor om vård och läkemedel för besvären i nacken

16. Redovisa nedan vilken vård/behandling du har sökt för besvär i nacken **de senaste 6 månaderna**:

a) Sjukgymnast

☐

Nej

☐☐

Ja

☐

-om Ja ange antal besök

_____ b) Naprapat ☐ Nej ☐ Ja -om Ja ange antal besök
 _____ c) Kiropraktor ☐ Nej ☐ Ja -om Ja ange antal besök
 _____ c) Osteopat ☐ Nej ☐ Ja -om Ja ange antal besök
 _____ e) Massör ☐ Nej ☐ Ja -om Ja ange antal besök
 _____ f) Läkare ☐ Nej ☐ Ja -om Ja ange antal
 besök _____
 _____ g) Annat ☐ Nej ☐ Ja -om Ja ange antal
 besök _____
 -om Ja ange
 vad: _____

_____ g) Annat ☐ Nej ☐ Ja -om Ja ange antal besök

 -om Ja ange
 vad: _____

_____ i) Utredning i form av röntgen el liknande
☐ Nej ☐ Ja -om Ja ange antal besök

 -om Ja ange
 vad: _____

17. Vilka läkemedel/naturläkemedel och hur ofta har du konsumerat som direkt följd av besvären i nacken

de senaste 6 månaderna?

a) Naturläkemedel:

☐ Aldrig ☐ Ibland ☐ Dagligen

Vilket/vilka? _____

b) Receptfria läkemedel?

☐ Aldrig ☐ Ibland ☐ Dagligen

Vilket/vilka? _____

c) Receptbelagda läkemedel?

☐ Aldrig ☐ Ibland ☐ Dagligen

Vilket/vilka? _____

Frågor om din hälsa

	Mycket				
	Utmärkt	god	God	Någorlunda	
Dålig	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

18. I allmänhet, skulle du vilja säga att din hälsa är:

EQ-5D

Markera, genom att kryssa i En ruta i varje nedanstående grupp för det påstående som bäst beskriver ditt hälsotillstånd idag:

19. Rörlighet

Jag går utan svårigheter	<input type="checkbox"/>
Jag kan gå men med viss svårighet	<input type="checkbox"/>
Jag är sängliggande	<input type="checkbox"/>

20. Hygien

Jag behöver ingen hjälp med min dagliga hygien, mat eller påklädning	<input type="checkbox"/>
Jag har vissa problem att tvätta eller klä mig själv	<input type="checkbox"/>

Jag kan inte tvätta eller klä mig själv ☐

21. Huvudsakliga aktiviteter (t ex arbete, studier,
hushållssysslor, familje- och fritidsaktiviteter)

Jag klarar av mina huvudsakliga aktiviteter ☐

Jag har vissa problem med att klara av mina vanliga aktiviteter ☐

Jag klarar inte av mina huvudsakliga aktiviteter ☐

(
Vänd)

22. Smärtor/besvär

Jag har varken smärtor eller besvär ☐

Jag har måttliga smärtor eller besvär ☐

Jag har svåra smärtor eller besvär ☐

23. Oro/nedstämdhet

Jag är inte orolig eller nedstämd ☐

Jag är orolig eller nedstämd i viss utsträckning ☐

Jag är i högsta grad orolig eller nedstämd ☐

24. Termomterliknande skala

På denna sida har Ditt bästa tänkbara hälsotillstånd markerats med 100 och Ditt sämsta tänkbara hälsotillstånd med 0.

OBS dessa sista 6 frågor är EQ5D och då har vi bifogat det pappret när vi har skickat per post!